THE NEUROLOGIC AND PSYCHIATRIC ASPECTS OF THE DISORDERS OF AGING

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THE NEUROLOGIC AND PSYCHIATRIC ASPECTS OF THE DISORDERS OF AGING

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PREFACE

The broad general topic originally selected by the Trustees for the Thirty Fifth Annual Meeting of this stimulating Association was The Neurologic and Psychiatric Aspects of the Disorders of the Aged This title was of course a reflection of growing concern with the demographic, sociologic economic, and medical problems created by the scientific ad vances of the past century more particularly of the past four decades These have resulted in a rapid increase in average life span and a cor responding increase in the proportion of the population over the age of 65 who are therefore increasingly affected by the physiologic changes of aging and the degenerative diseases of later years From both physiologic and pathologic points of view the nervous system is unusually and es pecially importantly involved in this situation and the problems imposed on neuropsychiatrists are therefore legion

The Program Committee however made one slight but very significant change in the wording of this Session s topic For the words *of the Aged* they substituted the words *of Aging* Their purpose in doing so was a strong conviction that students of medicine—that is to say research workers and investigators who are the spearhead of advancement of knowledge—should adopt a dynamic rather than a static approach They particularly must think in broad general terms of biology Their interest is not so much in the broken down derelict end product of senility and degenera tion but far more in elucidation of how the poor aged wreck got the [illegible]

[illegible] The Program Committee and the essayists ap proached their problems from the point of view of the important differ ences between the neuropsychiatric problems of the aged and the more fundamental problems of aging The latter begins inevitably with the fertilization of the egg Inextricably entangled with the [illegible] of [illegible]

The read [illegible]
Committee [illegible]
[illegible] members of the Association who attended the meeting seemed unexpectedly favorably impressed

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CONTENTS

CHAPTER I

BIOLOGY OF AGING CELLS

ALBERT I LANSING

Aging means very different things to different people To the biologist aging is a process of unfavorable change in any adult organism usually correlated with the passage of time To the clinician aging is the summation of degenerative diseases in elderly humans including cancer, cardiovascular disease arthritis and many mental diseases To the social worker and sociologist aging is associated with the post retirement age individual who is in financial straits emotionally insecure inadequately housed and generally unwanted and unneeded by society To the individual woman aging means the loss of physical attractiveness to her aging is a cosmetic problem To the individual man aging means little more than loss of sexual potency I will in this discussion adhere to the biologist s concept of aging

From the point of view of the biologist a sharp distinction should be drawn between the process of aging or senescence and the state of being aged or senility Senescence is a process of progressive deterioration of the adult organism which is correlated with the passage of time and which terminates invariably with death of the individual One indeed might speculate that senescence is a process of progressive loss of the ability to live on the part of the adult Senility then would be the state of adulthood in which the ability to live has been significantly reduced There are of course degrees of enfeeblement or loss of vital capacity The thirty year old exhibits moderately reduced sexual vigor subtly diminished stamina and inability to perform maximally in tasks such as *professional* boxing The forty-year-old is more clearly inadequate Without elaborating in detail he is prone to accumulate fat his physical capacities are clearly reduced his vision is deteriorating and his susceptibility to degenerative diseases is appearing He deals with environmental changes in a manner quite d [illegible]

most er [illegible]

suit hi [illegible]

is crus [illegible] he has had many painful battles with environmental changes He has experience has learned to compromise with or adapt to environment This is wisdom it is also an expression of fatigue The fifty sixty and seventy year-olds are much like the so-called middle aged man except that the enfeeblement is progressively more manifest

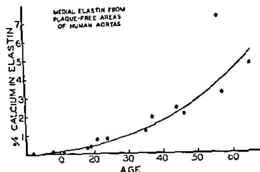


Fig 1.1 Age variations in calcium content of elastin in the media of human aortas grossly free of atheromata Calculated on a dried defatted basis (From Lansing Ann Int Med *36* 39 1952)

Again, if the same reasoning is applied to evaluation of age pigments one would conclude that these are not a product of aging because they occur in persons in their thirties The fact is that they are essentially absent in cells of individuals in the first few decades of life, make their appearance in the early thirties, and increase steadily with age thereafter Age pigments are a product of aging and highlight my point that aging begins rather abruptly at the time of maturation of the individual

These age pigments are especially attractive to the biologist who believes that the aging of the various forms of life including man have a common denominator Age pigments occur in plants, in invertebrates, in birds in the several mammals that have been studied, and in man

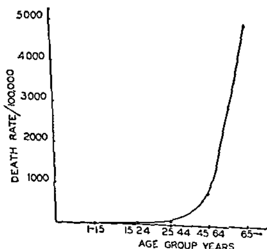


Fig 1.2 Death rate from cardiovascular disease in the United States in various age groups (Plotted from Dublin's data *Length of Life*, 1949 Roland Press N Y)

We are as I see it dealing with a mechanism which progressively reduces the adult s capacity to live The mechanism is operating in the thirty year old as well as the seventy year old I am disturbed that cur*rent interest in gerontology is restricted almost entirely to the terminal* stages of senescence Our population structure is rapidly shifting so as to contain more and more elderly people Because the elderly constitute a severe social and economic problem our governments both federal and local have suddenly discovered that aging is a problem Unemployability of the middle aged and compulsory retirement for the elderly have resulted in economic distress in an increasingly large cross section of our population This group of older citizens is difficult to cope with it is articulate experienced in dealing with problems and above all it is franchised They must be kept busy they need living quarters and money must be put in their pockets without compromising the manpower pool Our social workers and economists have a real Gordian knot to untie

On the health front it is clear that the degenerative diseases of later years are rapidly becoming the major problems of medicine Infectious diseases have to a large extent been conquered so that more of us live long enough to encounter crippling arthritis cardiovascular diseases cancer and diseases of the nervous system The latter may not be unique to old age but certainly show *an increased incidence in later years* As more people live long enough to enter into late adulthood medicine obviously will be compelled to concentrate its efforts still further on characterization *of the degenerative diseases These problems as well as those in the socio* economic area are very important but it should be recalled that they focus too sharply on the terminal porton of the life span Aging is a problem *of early and middle adulthood as well as of late adulthood and senility*

While I do not wish to deprecate the problems that beset the senile I do believe that it is a strategic error to focus too much attention on a narrow band of the broad spectrum of the problem of aging *To deal* solely with the narrow band is to invite garbled notions At the moment many consider arteriosclerosis not to be a problem of aging because this degenerative disease occurs in young people (those in the fourth decade of life) If however the individuals in this age group were actually beginning to age the attack on the problem of arteriosclerosis would be quite different A graph (fig I 1) prepared from Dr Dublin s data (*Length of Life* 1949) illustrates the death rate due to cardiovascular disease in various age groups It seems apparent from the graph that deaths due to cardiovascular diseases become a serious factor in early adult life *Similarly* if one examines data for the relation between age and calcification of medial elastic tissue in human aortas (fig I 2) free of atheromatosis it becomes evident that this process has its beginning at roughly the age of twenty

the work of Payne on endocrine organ changes with age in the fowl According to him the granular mitochondria in the basophils of the anterior pituitary gland gradually become vesiculated These vesiculated mitochondria increase in size perhaps by fusion to become enormous These bodies are not unlike age pigments In a recent electron microscopic study of age changes in spinal ganglia of the guinea pig Hess has found a close association between obvious age pigments and mitochondria The possibility exists that age pigments are the end product of mitochondrial degeneration

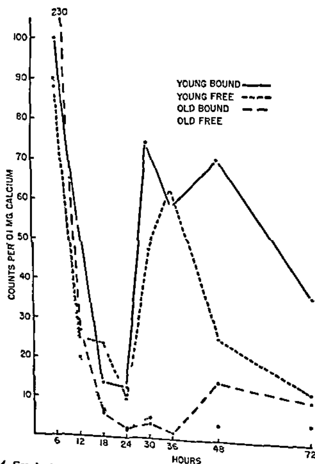


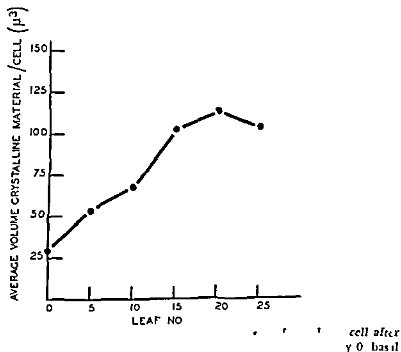
Fig 14 Graph showing the changes in specific activity of free and bound calcium (Ca^{*}) of young and old mouse liver after injection of radiocalcium (From Lansing Arch Biochem., 20 125 1949)

They are found in liver adrenal glands cardiac muscle anterior pituitary glands nerve cells etc

As early as 1891 Hodge called attention to age pigments in nerve cells of the honeybee and in cells of dorsal root ganglia of man Some theories of aging lean on the presence of age pigments and other cellular inclusions for evidence to support the idea that aging is a product of accumulation of metabolic by products in the cell For such inclusions to be toxic as these theories hold one would expect them to be reactive Yet the limited volume of chemical data on age pigments would indicate that these materials are remarkably insoluble

According to Jayne s recent work the acid fast age pigments in human cardiac muscle appear in the second decade of life and increase steadily with age thereafter they are insoluble in acids alkalis and fat solvents Their insolubility would suggest that they are probably inert in the cell It is worthy of note here that calcium compounds quite generally tend to increase with age It is well known that many salts of calcium are quite insoluble Perhaps age pigments and calcium salts because of their insolubility accumulate in the cell as they form simply because of lack of a mechanism for elimination of such materials

A clue to the mechanism of formation of age pigments is contained in



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They are consistent with the possibility that aging is an endogenous mechanism. Even this point is not clear, on the basis of existing information aging could quite conceivably be a product of endogenous or exogenous factors More research is needed

DISCUSSION

See Chapter II

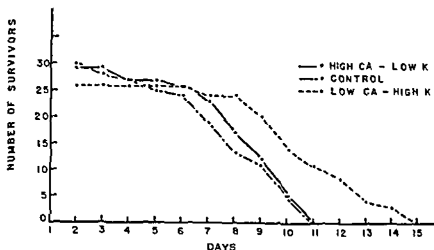


Fig 1 5 The effect of calcium concentration of the culture medium on the duration of life of Rotifer vulgaris (From Lansing J Exper Zool, *91* 195 1942)

In a number of publications I have suggested that calcium may play a significant part in the aging process Calcium increases with age in a variety of plants, invertebrates mammals, and in man In the cells of the water plant, Elodea, the calcium increase with age may be quantitated by *measuring the number of calcium oxalate crystals formed in the cell after* stimulation (fig 1 3) Microincineration as well as quantitative analytical procedures reveal a calcium increase with age in the soft tissues of various animal forms At least one isotopic study using Ca^{45} would indicate that old mouse liver is capable of taking up large amounts of calcium, particularly in the bound fraction The calcium that is bound in old liver is not as labile as that of young liver, its turnover is much lower (fig 1 4) The region of the cell cortex shows age increases in calcium content and longevity of rotifers can be extended by calcium deprivation (fig 1 5) Since calcium lowers cell permeability it is possible that the age change in calcium content results in reduced cell permeability It is tempting to speculate that this reduced permeability, if it does occur, may account for the accumulation of materials in the cell Unfortunately, there have been too few permeability studies to indicate whether or not there is a general change with age in this vital cell function Benedict inferred from his plant studies that there is a permeability decrease with age in *Vitis vulpina* but the method used *was too indirect to be taken seriously In some unpublished* studies on toad muscle several years ago I found that the rate of water loss or gain in solutions of various osmotic concentrations was age dependent Further studies like these are needed

These are a few of the cellular factors in aging that have interested me

velopment is not compressed into a separate formative phase of life but is coextensive with the whole life span continuing from egg to death even though with declining prominence and since much of what we call aging is but a special aspect of development—the reverse side of the same coin—our concept of aging must be correspondingly adjusted. The notion of a neuron ever being truly completed in the sense of a finished machine is as you shall see an illusion Development involves continuous transformations Like other cells live neurons can retain none of that precise detailed and durable stability of structure equipment and geometry that the printed stereotypes of our textbooks of microscopic anatomy have conjured in our minds Of course we all realize that no two cells even of the same type are ever nearly as much alike as are their five thousand identical illustrations in five thousand copies of the same textbook But what we do not commonly realize is that not even any given cell is quite the same today as it was yesterday indeed it changes much more in one day than its textbook effigies have changed in many decades of transit from one text to another The neuron is in perpetual flux of concurrent degradation and renewal This instability renders it mutable both in adaptive and regressive directions And since this aspect of the life history of the neuron has much potential impact on problems of aging I shall devote the substance of my further account to it.

That the neuron as a whole is not a stable but rather a stationary unit is a relatively recent discovery There has been prior recognition of instability on the molecular level below and of plasticity on the supracellular level above On the molecular level the extensive work with isotopes has revealed the unsuspectedly rapid turnover of protoplasmic constituents On the supracellular level those theories at least that try to refer phenomena of association memory and adaptive behavior to changes in the pattern of the neuronal network *for to mod* [illegible]

[illegible] the plastic web of connections But now even this intermediate *island of solidity* has lost its former aspect of fixity In this regard it falls in line with *other* protoplasmic systems in the body that are destined to last for life In order [illegible]

their [illegible]

drain

[illegible]

To [illegible] look at a column of skin reaching from the basal layer of the epidermis to its surface (fig II 1 top) Normally only the cells at the base can grow and reproduce They turn food stuffs into

CHAPTER II

THE LIFE HISTORY OF THE NEURON

PAUL WEISS[1]

There was a time not so long ago when the life history of a neuron could have been described about as follows a primitive cell derived from the actively proliferating neural epithelium of the embryo wanders off into the mantle ceases to divide enlarges sprouts an axon then dendrites forms synaptic connections with other cells neural or non neural enlarges further receives end feet from other neurons develops in quick succession a series of enzyme systems (7) enlarges still more deposits Nissl bodies in its cytoplasm and at last is turned over to its user—the finished body—like a machine come off the assembly line essentially in ready working condition just to be run in polished and improved in its wiring This description as you note grants to the neuron as to the machine only a strictly limited epoch for its construction—called development—which in a standard mammal would occupy no more than about the first one per cent of the total life span During the remaining ninety nine per cent the owner would have to get along with the physical equipment previously received as a static and immutable apparatus Once the embryonic assembly plant had been dismantled no worn out parts could be replaced no major repairs executed

Evidently this concept of a life history sharply divided into a formative and an operative phase has had a profound effect on our concept of aging Machines too age and principally from three causes material decay—as when stone weathers or rubber rots deposition of foreign matter—such as grit or sludge or slags and ordinary wear and tear—which means the cumulative record of nicks and abrasions accentuated by insults and negligence in use all of these pointing to the scrap heap Naturally under the spell of this machine analogy one has taken a similar fate of the neuron for granted Partial to microscopic signs one readily accepted certain insoluble pigment granules that pile up in ganglion cells with age as visible evidence of such functional impairment

Yet more recent insight into the processes of development calls for a rather thorough reorientation of our thinking about such matters De

[1] From the Rockefeller Institute for Medical Research New York Work aided by grants from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council and the National Institutes of Health Public Health Service

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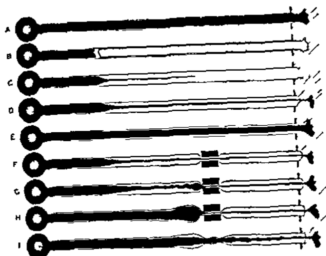


Fig II 2 Diagrams of single nerve fibers in ordinary regeneration (*B E*) and in regeneration combined with constriction (*F I*) in the last case (*I*) followed by later release of the constriction (From Weiss and Hiscoe)

ing diagram (fig II 2) summarizes the results of six years study involving experiments and observations on more than one hundred thousand nerve fibers (24)

You see here nine mature neurons a normal one on top the others in various stages of ordinary or modified regeneration The nucleated cell bodies are on the left the periphery is on the right Lines B to E recapitulate the regenerative events following the crushing of a fiber

The proximal stump issues a thin filamentous outgrowth which advances through the distal degenerated portion into the periphery (as seen in C) where it makes connection with an old degenerated end organ as in D The new sprout is then still very thin Only gradually does it enlarge in width eventually approximating full caliber To achieve this it must grow in protoplasmic mass about a hundred fold

It was this increase in girth which formed the subject of our investigations By placing a constriction around a nerve we can red

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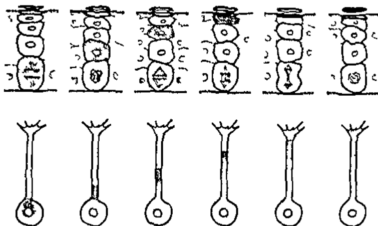


Fig II 1 Diagrams of the mode of growth of a column of epidermis (top) and of a neuron (bottom) A newly produced mass of protoplasm (stippled) is followed through six progressive stages from left to right to its final disposal

more protoplasm of their own kind, and when they have grown to twice their size, they divide, one cell retaining its basal position and reproductive function while the other cell is pushed up one story It soon is raised another story as the next cell is added from the base while it in turn crowds the more outer cells The column thus would keep on rising save for the fact that in their rise the cells become progressively transformed into plain keratin in which form they flake off the free surface As long as the loss at one end and the gain at the other are equal the column keeps a constant stationary height Whenever production exceeds shedding the height will grow the skin becomes thicker conversely when shedding out strips reproduction the column will shrink

Now but for the facts that in the skin the growing basal cells also divide and that the discard at the other end is visible the column of skin cells is quite comparable to a single neuron with the nucleated cell body or perikaryon corresponding to the base of the epidermal column (fig II 1 bottom) For in the neuron likewise it is at this pole that protoplasm is continuously reproduced then passed on to the rest of the neuron where it is *dissipated albeit in molecular hence less tangible form* Just as in the skin column the size of the neuron at any one moment therefore will only be an expression of the momentarily prevailing ratio of production over dissipation and will remain constant only as long as the two opposing processes are in equilibrium

Thus the difference between the steady state of skin blood and glands on the one hand and of neurons on the other is simply that in the former both loss and gain are grossly visible as cell destruction and cell division respectively whereas the neuron is less ostentatious Just by a lucky accident did I discover microscopic signs of its perpetual growth The follow

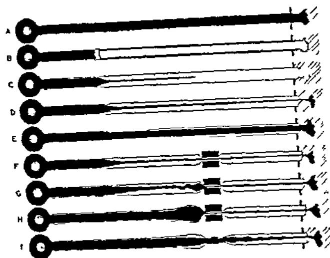


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It was this increase in girth which formed the subject of our investigations By placing a constriction around a nerve, we can reduce the caliber of each constituent nerve fiber locally, as shown in lines F, G and H If now we cut the fiber proximally to the constriction a thin filament again regenerates through the constriction (in F) But as this filament keeps enlarging and attains the diameter of the constricted portion a marked asymmetry begins to appear between the portions of the fiber lying proximally and those distally of the constriction as you can see in G and H The distal portion remains thin and permanently so while at the proximal end of the constriction surplus neuroplasm piles up Conclusion the growth of the axon evidently occurs solely from its base, and the constriction, acting

as a bottleneck, has throttled the supply of growing mass to the distal portion

Now, it is most important to understand precisely just how this growth occurs and what it implies In the first place, this is not simply a matter of pumping the distal fiber full of axonal substance, like distending a hose If it were the piece distal to the bottleneck would only take longer to attain full size but eventually it would attain it However, in reality it never does it stays forever nearly as thin as the bottleneck itself It thus compares *rather to a leaky hose being inflated That is its substance continues to* suffer the drain of local metabolic consumption while the replacement stream from the remote central source is slower in compensating for the loss because of the narrowed passage

Secondly while proximo distal convection of some prerequisites for axonal maintenance had indeed been postulated by Cook and Gerard (5) and by Parker and Paine (16) this does not accurately express the situation For what is conveyed from the cell to the axon is not a flux of essential supplements for local growth—for instance enzymes for distal protein synthesis—but is a coherent column of finished axonal substance As has been conclusively demonstrated by the qualitative and quantitative analysis of the configurations and deformations assumed by the axons at the central side of the constriction the whole axon is in centrifugal motion

The most dramatic evidence of this steady propulsion is obtained when the constriction is removed many months after the system has come to equilibrium One can then directly follow the dammed up protoplasmic surplus on the near side of the constriction forcing its way down through the widened passage like a dammed up stream through opened flood gates on into the far portion of the fiber (see line I of diagram) The distal fiber segment of a constricted fiber may have been undersized for a year or more and still resume larger caliber upon release of the stricture as axoplasm can now enter with a broader front (22) Such a released axonal flood wave advances at the rate of several millimeters per day which may be taken to be *the order of magnitude with which the axonal column normally grows* forth from its central base If the liberation of ammonia from nerve is taken as a measure of the complete break down of protein in the peripheral portions one would have to postulate a rate of replacement from the central supply source of the same order as that actually observed for the advance of the axonal column (21)

Finally this axonal movement is by no means confined to phases of regenerative regrowth of a fiber, but is a permanent feature of neuronal life For instance if a partial constriction is placed in a full sized mature nerve fiber without disrupting it the distal part though still connected with the cell body, gradually shrinks in accordance with the reduced entry of new

axonal mass it returns to its former dimensions whenever the obstruction is again removed

What happens, evidently, is that new neuroplasm, produced continually in the nucleated territory of the cell, enters from there a sort of conveyor belt that moves it down into the periphery On its way, it is then progressively consumed in the replacement of degrading protoplasmic systems, and the size of the neuron at any one time is simply a measure of the then prevailing ratio between overall consumption and renewal from the central source Thus returning once more to the stationary column of epidermal cells (fig II 1), we find it truly illustrative of the neuron, except for the fact that the latter does not divide and dissipates its substance diffusely, rather than in one terminal package

More indirect confirmation of the continuous growth of the *neuron* has come from the cytochemical investigations of Hydén (12) and collaborators, who deduced a high rate of protein synthesis in the cell from the elevated *nucleic* acid concentration in and around the nucleus Equally pertinent is the report from Gerard s laboratory (17) that labelled phosphoprotein seems to shift peripherad in nerves at a rate of more than 2 millimeters per day which corresponds closely to the measured rate of axonal advance in our experiments

After all this the neuron now appears in a wholly new light Divested of its simulated structural fixity it assumes the wide latitude of adaptive expression open to a system *in* steady flux Evidence for such adaptations, both of size and substance, is rapidly accumulating Far from being set, size goes up or down with fluctuations in the rate of synthes [illegible]

[illegible] existence of peripheral connections Un connected neurons do not attain their full mass (13) A mature neuron, whose connections have been severed secondarily [illegible]

[illegible] When reconnected with a peripheral organ the neuron gains again If it is overloaded with additional branches and connections, its nucleus and cell body assume dimensions far in excess of normal (4, 6) The production center of the neuronal mass thus conforms to the demands of the peripheral innervation volume

Similarly it adjusts itself to functional [illegible]

relative mass in retinal cells presumably is also a functional effect of illumination for it does not take place in the dark (2) When the ganglion cells in the antidiuretic center in the hypothalamus are overactive in thirsting animals then hyperfunction likewise entails enlargement of the nuclei and nucleoli (15)

Our main point here is that because the neuron is not a settled fixture in the mechanical sense because not only its interstices and surfaces but the entire system is in a state of perpetual reorganization its size remains greatly variable throughout life

One could hardly assume that such wide fluctuations would leave unaffected the subtle connections of other neurons that end on the expanding or shrinking surface of the variable cell body Just how the density and distribution of end feet and other relevant synaptic features would change remains to be determined But there can be little doubt that the relation between function and the size of the cell body is mutual that not only does the cell body adapt its dimensions to the actual functional load but that the resulting change of size will reciprocally affect some functional parameters

To these quantitative changes must then be added the possibility of major qualitative adaptations to extraneous conditions developmental trophic functional or otherwise Much of my early work amply confirmed and expanded since by Sperry (20) has clearly revealed that a neuron switched to a different peripheral termination can adopt the specific character and central response relations of its new end organ There is some evidence though that this adaptive faculty for qualitative modulation declines with advancing age (18) hence its scope during later life is quite uncertain

The biochemical basis of these qualitative modulations is much too subtle to be detectable by methods of current cytochemistry However those qualitative cytochemical changes that are directly demonstrable are by their very grossness indicative of the profound variability in its chemistry of which the neuron is capable The well known depletion of Nissl bodies during high activity has now been identified with a marked decrease of ribonucleic acids (11) At the same time a conspicuous increase has been noted in the lipids of hyperactive ganglion cells (Purkinje cells of rabbits following prolonged rotation Hydén 1961)

Whatever all these changes may mean functionally for us they signify that neuroplasm is subject to ceaseless change of composition throughout life Let us examine what this implies

The mechanisms of protoplasmic reproduction are still very obscure but this much seems assured 1) *Gene replication is basically involved* 2) The complement of genes remains essentially the same in all cells of all

somatic types 3) Differentiation on the other hand connotes divergence of physical and chemical constitution in different cell types

To reconcile this last fact with the thesis of gene constancy, one must assume that the extragenic protoplasmic systems of nucleus and cytoplasm assume divergent patterns and that these latter then evoke different interactions from the same group of genes or as I have suggested convert common gene products into cell type specific compounds by serving as models or templates (19 21) In this way the cytoplasm can impose its pattern on substance newly procreated from genic sources in the nucleus Accordingly if the relevant molecular pattern in the cytoplasm undergoes changes all subsequently reproduced mass would be cast into the changed mould as it were so that the changed configuration would be perpetuated

Thus as the neuron keeps renewing its substance the pattern of this renewal may undergo significant alterations during life Some of these changes may be of the slow autonomous kind often referred to as maturation but there might also be others that are induced from the outside comparable to the phenomenon of adaptive enzymes Many microorganisms can learn to metabolize unusual substrates and to pass this acquired faculty on to their offspring as long as the changed substrates are present (14) If this kind of self perpetuating modification were equally common in tissue cells for which there is as yet no proof then obviously the neuron being in continous self reproduction might perhaps be a case in point

Let us now summarize I have tried to show that the life history of the neuron cannot be written in static terms It is a *history of flux* What used to be viewed as stable *products* has revealed itself as a steady flow of *production* change in *equipment* as a change in the *reproductive pattern* Aging therefore would be not so much a matter of gain or loss of physical equipment as a matter of inadequacies and incongruities arising in the renewal process with the consequent decline of the adaptive features which that process sustains If one insists on using a machine analogy the machine that fails primarily in *aging is not the* physiologic machine which operates the *nervous* system but the *developmental* machine which keeps that physiologic machine in good repair The enormous complexity of the network of interactions essential for this process should caution us not to expect any one master reaction to hold the key to the understanding of neural aging To add to the *complexity* you must bear in mind that the life history of the neuron is moreover intimately connected with the life histories of the neuronal accessories especially glia and sheath cells which I have not even touched upon—largely because even less is known about them Now the resolution of complexity lies not in arbitrary simplification but in the patient disentangling of the complex fabric The threads I

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Our main point here is that because the neuron is not a settled fixture in the mechanical sense, because not only its interstices and surfaces, but the entire system is in a state of perpetual reorganization, its size remains *greatly variable throughout life*

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To these quantitative changes must then be added the possibility of major qualitative adaptations to extraneous conditions, developmental, trophic, functional or otherwise Much of my early work, amply confirmed and expanded since by Sperry (20), has clearly revealed that a neuron, switched to a different peripheral termination, can adopt the specific character and central response relations of its new end organ There is some evidence, though, that this adaptive faculty for qualitative modulation declines with advancing age (18), hence, its scope during later life is quite uncertain

The biochemical basis of these qualitative modulations is much too subtle to be detectable by methods of current cytochemistry However, those qualitative cytochemical changes that are directly demonstrable are, by their very grossness, indicative of the profound variability in its chemistry of which the neuron is capable The well known depletion of Nissl bodies during high activity has now been identified with a marked decrease of ribonucleic acids (11) At the same time, a conspicuous increase has been noted in the lipids of hyperactive ganglion cells (Purkinje cells of rabbits following prolonged rotation, Hyden, 1951)

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In any event one does have evidences of all sorts of a decreasing turnover a decreasing speed a decreasing activity with age and I completely subscribe to the point of view that Dr Weiss developed Aging is essentially a failure of the regenerative the reconstitutive or the rejuvenative processes and I would like to take my remaining minutes to ask first why is this failure inevitable and second what does it mean in the nervous system?

The answer to the first question I should say is that it is not inevitable If there were not some counter action organic life could not endure let alone build up by evolution This revitalizing event happens in endomixis or the sex exchange in organisms and suddenly renews completely the total vital potential—whatever I mean by that—so that the life processes get wound up over and over and over again One can duplicate this less mysteriously by other maneuvers such as repeated starvation of lower organisms which leads to repeated rejuvenation and prolongs life apparently indefinitely

In the case of the central nervous system it seems to me that this whole question is intimately tied up with that of regeneration and rejuvenation Most people are now at last convinced that regeneration of fibers in the central nervous system is possible It has been established many times The effectiveness of this falls off rapidly with aging but apparently regeneration can again be hastened or accelerated by a variety of techniques What is not yet generally realized is that adult neurons can divide can undergo mitosis and reproduce themselves and so in effect can regenerate In tissue culture this has been done with pyramidal cells of the human cortex and there is then potentially the possibility even of restoring whole neurons in the nervous system We merely must learn how to do it

The problem in neural regeneration is to find those processes devices or agents which will bring about a rejuvenation or anti aging [illegible]

[illegible]

[illegible] a rotated eye acts on the basis of an upside down view of the world for the rest of its life A rejuvenating action on the nervous system might restore the ability to adapt and cause such a frog say to jump toward rather than from a fly The return towards normal of a reversed behavior would thus directly test how electro- or drug shock insulin hyperthermia cortisone or any other maneuver is able to bring about a regenerative reorganization of the nervous system

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have tried to extricate here are but a modest few, yet they seem to lie close to the core of the perplexing problem of aging

DISCUSSION

DR RALPH GERARD [Ann Arbor Mich] These two papers have presented a rich and broad lens picture of the whole problem of aging and as the Chairman has already said were a splendid opening to the meeting

It occurred to me that it would be of some interest to try to extend the thinking more particularly to the nervous system *and to examine the changes of aging and the mechanisms* for these and then to generalize in regard to the large question is aging necessary and what can be done about it at least in the case of the nervous system?

The phenomena of aging that relate particularly to the nervous system include slower learning a greater rigidity in what one knows with less willingness to shift views and a decrease of recent memory The loss of recent memory is an example of the steady process of slowing down and rigidification There is also a quantitative loss of functioning—of acuity on the sensory side of speed and power on the motor side

Now what kinds of mechanisms are responsible for these changes? First although the phenomena I have pointed to are primarily in the nervous system they exemplify *more general changes involving the protoplasm of cells throughout the organism* I shall never forget some sea anemones at the Marine Station in Naples They were protected and lived far beyond the normal life span of sea anemones They were much larger than any found in the open and were so rigid—from the actual deposit of stiff material the loss of water and all the other changes of aging—that their tentacles could barely be moved fast enough to ingest sufficient food for life The over all slowing process is very dramatic

Second what are the more particular mechanisms in the nervous system involved in these changes? Whatever they are there is less a breakdown of function than a limitation in span An octogenarian story makes the point well The old gentleman in some *way insulted about his decreasing powers pulled himself up to full height and said* I ll have you know I m just as good a man as I ever was thought a moment and then added For one hour a day The mechanisms involved in this decay are at the cellular and the subcellular levels as the speakers have brought out—a particular neuron decreasing in size decreasing in metabolic rate increasing in the slag it carries I would suggest incidentally Dr Lansing that even though the granular particles may be completely nontoxic they may still like a stalled automobile in the road obstruct traffic and seriously hamper the functioning of neurons The binding of calcium and the accumulation of metaplasm can certainly slow function and I hope that subsequent papers will deal with the falling metabolism of neurons with age There is also a loss *of cells during aging* many reports indicate a decrease in absolute number in the muscle receptor and neuron populations

Conversely a filling up of the dendritic field is noted If new processes progressively fill the total capacity so that further fiber or dendrite growth becomes difficult and finally impossible this may have something to do with the failure of recent learning The problem of the actual changes in the connections the patterns of the neurons is implied by several of the important facts that Dr Weiss presented Incidentally Dr Weiss if one *makes the assumption that there is a balance between loss of material* at the periphery of a fiber and inflow of material through the constriction and that loss depends on surface the radius of the peripheral fiber should vary as the square of the radius of the constriction I don t suppose that your data are sufficiently precise to say whether or not that is true That the whole axon grows continuously with a steady

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CHAPTER III

BRAIN METABOLISM IN RELATION TO AGING

HAROLD E. HIMWICH AND WILLIAMINA A. HIMWICH

There is a general agreement that an impairment in the efficiency of mental as well as of physical powers occurs in old age In some, this impairment is delayed longer than in others and in any case the difference is less noticeable in individuals whose intellectual capacities are well developed. What are the underlying changes in the brain which may give rise to such deteriorating alterations? It will be the main purpose of this paper to ascertain the biochemical changes in the brain associated with old age in an effort to correlate them with the alterations in behavior which may occur in the last period of life

One method of study is to measure the cerebral metabolic rate Long years of experience have proved that basal metabolic rate, or the oxygen consumption of the entire body, gradually falls after 40 years of age and more swiftly so after 80 years There is evidence that cerebral metabolic rate also declines in old age

But for the sake of completeness and to set the background for further discussion we shall reiterate that cerebral metabolic rate is reduced in aged individuals (1) The decrease in metabolism is dependent chiefly upon a retardation of cerebral blood flow and the latter is associated with an augmented cerebral vascular resistance (2 3) Why is this retardation of blood flow not compensated for by a relaxation of cerebral vascular resistance? It has been shown that even in the aged cerebral blood flow can [illegible]

[illegible] cerebral blood flow by a compensatory relaxation of cerebral vascular resistance? There would seem to be another factor perhaps that of parenchymal damage and the diminished oxygen consumption of the brain would then be secondary to alterations in brain cells (5) Thus the cells may not only suffer injury as a result of the impaired blood supply but there may be a direct action on the cells by some toxic product so that parenchymal damage may accrue In that case the low cerebral metabolic rate could be secondary to prior damage of the brain cells It is of interest that there seems to be a similar decrease of metabolic rate whether or not the patients reveal abnormal behavior (6) Aged individuals who are apparently normal have cerebral metabolic rates like those of elderly persons with signs of psychotic or neurologic dis

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TABLE III 1

Respiration of Rat Brain Homogenates in Relation to Age (from Reiner (11))

	Age (Months)							
	Embryos	0-1	1-4	4-6	6-12	12-18	18 24	Greater than 24
QO_2 dry weight	10	14	15	16	15	16	15	10

metabolic rate has been reduced to such low values as are seen only in embryonic life (table III 1)

If we accept a reduction in cerebral metabolic rate as an accompaniment of old age we may regard it as another sign of altered biochemistry and seek other changes of the brain which can be correlated with such a decrease Let us turn first to an examination of the water content of the brain One of the most important constituents of the body in general, as well as of the brain is water Certainly it is greatest from a quantitative viewpoint and all the reactions on which life depends take place in an aqueous medium Donaldson (12) published observations on rats showing a decrease in the percentage of water content for the entire brain in the first year of life (table III 2) Other experiments made on rabbits up to 4 years of age approximately middle life are in agreement with such a decrease in moisture (13) In addition they disclose that the water content of the various parts of the brain examined reveal a phyletic order The newer parts of the brain cortical gray and caudate nucleus contain more moisture on a percentage basis than the superior colliculi and medulla oblongata These results suggestive as they are fail to give us information on what happens in human beings

At this point it may be well to emphasize that observations made on humans do not afford experimental conditions as satisfactory as those of animal experiments Let alone the fact that these brains have been frequently obtained from diseased patients and have undergone premortal changes including those of a period of coma before death in addition post mortem alterations must be considered for rarely is a brain taken immediately after death and the periods before autopsy are variable Further

TABLE III 2

Water per cent of rat brain in relation to age (from Donaldson (12))

	Age (Days)							
	Birth	10	21	31	41	100	250	365
Per cent of water	88 00	86 72	82 49	80 19	79 36	78 55	78 01	77 50

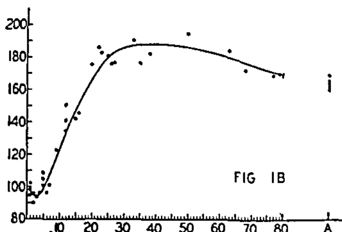


Fig III 1 Changes in oxygen consumption of rat brain from birth through maturity Age in days (abscissa) plotted against oxygen uptake cu mm O_2 per 100 mg tissue per hr (ordinate) Brain metabolism rises rapidly to a maximum at 1 month of age after which there is a slight but significant decrease (Reproduced by permission from Tyler and van Harreveld (7)

orders Whether or not the regressive changes are associated with clinical manifestations or are relatively silent depends upon the part of the brain where they are most prominent In any event a decrease of brain metabolism is a sign of aging and further support for this conclusion comes from observations of excised cerebral tissues The examination of brain metabolism in the various mammalian forms reveals a rapid postnatal rise followed by a slower and more gradual fall during the period of maturity This applies to the rat (7 8 9) and the dog (10) (Fig III 1) Unfortunately, none of these data was extended far enough into the life span to include the old age and for an obvious reason it is more difficult to get aged laboratory animals than younger ones

There is however one report in the literature (11) which estimates brain metabolism in the rat throughout a period of 3 years This is a ripe old age for that animal Unfortunately in this paper the oxygen consumption was reported on a basis of dry weight Although this method is frequently used it misses many of the variations of the early rapid rise of cerebral metabolic rate This failure is easily understandable since the water content rapidly falls at this time so both dry weight and oxygen consumption rise together Only on a moist weight basis can we observe the variations in the rates of metabolism per weight of brain tissue When changes in water content are taken into consideration cerebral metabolic rate is given in terms of the living tissue *i e*, in the terms of brain weight similar to those observed *in vivo* Despite this drawback in the method of estimating the oxygen consumption on a dry weight basis a fall of metabolism after two years of age is evident in Reiner s (11) observations In fact in the aged rats the cerebral

TABLE III 1

Respiration of Rat Brain Homogenates in Relation to Age (from Reiner (11))

	Age (Months)							
	Embryos	0-1	2-4	4-6	6-12	12 18	18 24	Greater than 24
QO_2 dry weight	10	14	15	16	15	16	15	10

metabolic rate has been reduced to such low values as are seen only in embryonic life (table III 1)

If we accept a reduction in cerebral metabolic rate as an accompaniment of old age we may regard it as another sign of altered biochemistry and seek other changes of the brain which can be correlated with such a decrease Let us turn first to an examination of the water content of the brain One of the most important constituents of the body in general, as well as of the brain is water Certainly it is greatest from a quantitative viewpoint and all the reactions on which life depends take place in an aqueous medium Donaldson (12) published observations on rats showing a decrease in the percentage of water content for the entire brain in the first year of life (table III 2) Other experiments made on rabbits up to 4 years of age approximately middle life are in agreement with such a decrease in moisture (13) In addition they disclose that the water content of the various parts of the brain examined reveal a phyletic order The newer parts of the brain cortical gray and caudate nucleus contain more moisture on a percentage basis than the superior colliculi and medulla oblongata These results suggestive as they are fail to give us information on what happens in human beings

At this point it may be well to emphasize that observations made on humans do not afford experimental conditions as satisfactory as those of animal experiments Let alone the fact that these brains have been frequently obtained from diseased patients and have undergone premortal changes including those of a period of coma before death in addition post mortem alterations must be considered for rarely is a brain taken immediately after death and the periods before autopsy are variable Further

TABLE III 2

Water per cent of rat brain in relation to age (from Donaldson (12))

	Age Days)							
	Birth	10	21	31	41	100	2 0	365
Per cent of water	88 00	86 72	82 49	80 19	79 36	8 [illegible]5	78 01	77 50

TABLE III 3

Total nitrogen content (grams per cent) of four different areas of cerebral gray matter of patient B age 69 years and of hemispheres of four rabbits (personal data)

Area	Patient	Rabbit Hemispheres
Frontal pole		
R	1 56	1 70
L	1 44	1 74
Other frontal area		
R	1 44	1 71
L	1 33	1 71
Temporal pole		
R	1 39	1 0
L	1 54	1 72
Occipital pole		
R	1 64	1 70
L	1 88	1 75

more in the presentation of these data mention was not made of which cortical areas were sampled Yet observations performed in this laboratory (14) disclose that the chemical contents of the cerberal cortex are not uniform but may vary from part to part (table III 3) It may be seen that not only do the nitrogen contents of different cortical areas vary but also symmetrical parts taken from the right and left hemispheres differ These results differ from those obtained on rabbit brain for in that animal the correspondence for the right and left sides is close You will observe that the total nitrogen contents of the right and left hemispheres of four different rabbits are in much closer agreement than of the right and left sides of the human patients (table III 3) The data on human brains therefore must be evaluated in terms of the conditions in which they were obtained

The work of Johnson McNabb and Rossiter (15) shows that the human adult brain exhibits a smaller concentration of water than that of the infant and that the decrease in water concentration is associated with the growth of the total lipids of the brain Unfortunately these results do not yield information on our particular subject of interest old age The data of MacArthur and Doisy (16) unlike the preceeding includes exact ages but go only as far as 67 years The observations of Brante (17) however extend to the brains of individuals up to 90 years of age Brante presents the values for the dry weight as per cent of wet weight of cortical gray and white matter (table III 4 (17)) Subtracting these results of dry weight per cent from 100 we obtain the per cent moisture content of the brain In table III 4 the results obtained from individuals of various age groups are averaged in an attempt to determine whether there is a trend in the changes of

TABLE III 4

Water content of cortical gray and white matter per cent fresh tissue in relation to age (from Brante (17))

Cortical Matter	Years					
	1	2-5	10-16	19-35	65-6	8-90
Gray						
No of brains	2	3	4	2	4	3
Water percentage	89	87	84	84	86	87
White						
No of brains	3	3	4	4	3	2
Water percentage	85	75	69	71	71	74

water content with age A rapid fall in water content from the first year of life to about 10 to 16 years of age is followed by a stage of stabilization with however a rise in the percentage of water in the brains of the oldest individuals studied We wish we had more data to test the idea as to whether the brain contains a greater concentration of water in extreme old age or stated differently suffers a decrease in solids With additional information we might find that the water content of the brain remains practically unchanged It is even possible that a fall in the water content of the brain occurs But we must take the available observations into consideration and it is therefore necessary to determine whether any relationship exists between the lipids of the brain and water as the lipids form a quantitatively important fraction of the dry weight of the brain

In order to compare Brante s (17) lipid data with those of water the former are also recalculated on a moist weight basis Table III 5 (17) c tains such a recal

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is seen rapid and then slower—to 65 to 6 years followed by a decrease from 78 to 90 In general the lipid contents of gray and white matter show the same order of alterations except that th e greater and the dif fer Table III 5 includes not p osphohpids cholesterol

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TABLE III 5

Lipids of cortical gray and white matter per cent fresh tissue human brain in relation to age (recalculated from Brante (17))

	Years					
	1	2–5	10–16	19–33	63–76	78–90
Gray matter						
No of brains	2	3	4	2	4	3
Total lipids	3.47	4.62	4.98	5.31	5.60	4.65
Phospholipids	2.14	2.68	3.12	3.28	3.12	2.50
Cerebrosides	0.36	0.51	0.36	1.04*	0.70	0.68
Cholesterol	0.54	0.70	0.75	0.80	0.81	0.68
White matter						
No of brains	3	3	4	4	3	2
Total lipids	7.54	13.66	18.72	18.00	18.10	15.10
Phospholipids	3.81	6.12	8.22	7.79	7.49	6.82
Cerebrosides	1.36	2.90	4.46	4.07	4.22	3.24
Cholesterol	1.50	3.04	4.50	4.93	5.01	3.67

* One value

tional data to determine whether or not the apparent hydration of the brain will be supported by further work

Germane to our discussion is the division between extracellular and intracellular water In 1916 Donaldson (18) wrote of the unique character of the nervous system to accumulate the greater fraction of its lipids outside the cell bodies in the form of myelin substances Thus while extracellular fluid decreases the relation between water and solids within the cell remains fairly constant The data obtained by Yannet and Darrow (19), on growing cats yield quantitative results in support of Donaldson s conclusions They found that the reduction in concentration of water which occurs with growth is due to a decrease in extracellular fluids Extracellular water decreases from 33.9 to 29.8 per cent while intracellular water remains unchanged within the error of the method going from 50.7 to 51.0 per cent Accordingly they note that sodium and chloride largely extracellular elements decrease, while potassium mainly an intracellular substance remains unaltered (table III 6) Yannet and Darrow (19) also note that the increase of nitrogen and phosphorus is chiefly dependent on the greater concentration of lipids

If the suggested hydration in old age is accompanied by a reduction in the concentration of total lipids and if the former is chiefly extracellular then the inverse relationship between lipids and extracellular water observed during growth may also hold for old age and the extracellular fraction may increase at that time However without available data on the in

TABLE III 6

Concentrations per kg of brain tissue of water nitrogen chloride sodium potassium, phosphorus and fat (from Yannet and Darrow (19))

Group	No of Rats	Water	Nitrogen	Chloride	Sodium	Potassium	Phosphorus	Fat
		gm	*gm*	*mM*	*mM*	*mM*	*mM*	*gm*
A	9	84 6 ± 5 0	14 7 ± 0 3	43 2 ± 1 4	55 1 ± 1 4	87 0 ± 1 6	76 9 ± 3 7	30
B	8	80 8 ± 4 0	16 8 ± 0 2	39 0 ± 1 0	52 5 ± 1 2	88 0 ± 2 2	96 3 ± 0 5	60

Group A includes animals weighing up to 800 gm Group B animals weighing from 800 to 2500 gm.

TABLE III 7

Rat brain protein (absolute weight in mg) in relation to age in days (from Donaldson (12))

	Age (Days)					
	1	10	20	40	120	210
Protein (mg)	15 14	60 45	119 40	136 00	165 20	177 00

organic metabolism of the aged brain and its water compartments, such a decision between extracellular and intracellular fluids cannot be [illegible]

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c [illegible] at the concentration of lipids becomes larger as the total fluids fall and this fall of fluids is due chiefly to a decrease in the extra cellular component Whether or not a reversal of this relationship takes place in the aged individual cannot be determined without additional data

Another important factor in the total solids of the brain is its prote[illegible] The increase of tot[illegible] is seen in table III [illegible] far enough to dra[illegible] changes in protein in old age and moreover they were obtained on rats Observations of human brain are supplied from the results of MacArthur and Doisy (16) We see again a rise throughout the life period almost reaching maximal values in the 21 year old adult and decreasing somewhat in the 67 year-old individual (table III 8)

A source of information on the protein concentration of the cerebral cortex is found in Brante s work (17) Protein content can be estimated from the differences between the weight of total lipids and the total dry weight Such values representing as they do all materials not soluble in fat

TABLE III 5

Lipids of cortical gray and white matter per cent fresh tissue human brain in relation to age (recalculated from Brante (17))

	Years					
	1	2–5	10–16	19–55	65–76	78–90
Gray matter						
No of brains	2	3	4	2	4	3
Total lipids	3.47	4.62	4.98	5.31	5.60	4.65
Phospholipids	2.14	2.68	3.12	3.28	3.12	2.50
Cerebrosides	0.36	0.51	0.36	1.04*	0.70	0.68
Cholesterol	0.54	0.70	0.75	0.80	0.81	0.68
White matter						
No of brains	3	3	4	4	3	2
Total lipids	7.54	13.66	18.72	18.00	18.10	15.10
Phospholipids	3.81	6.12	8.22	7.79	7.49	6.82
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If the suggested hydration in old age is accompanied by a reduction in the concentration of total lipids and if the former is chiefly extracellular then the inverse relationship between lipids and extracellular water observed during growth may also hold for old age and the extracellular fraction may increase at that time *However, without available data on the in*

of its protein content, for PNA (pentose nucleic acid) forms a pentose nucleoprotein The maintenance of normal neuronal function is associated with the production of pentose nucleoprotein and large amounts of that complex substance are found in the large nerve cell of the adult. What is significant for the present study is that the amount of PNA decreases with old age (22) X ray microradiography reveals that the parts of the brain containing pentose nucleoprotein possesses much less dry matter than areas *containing* a yellow pigment, a substance which accumulates in old age Thus the *nucleoproteins* are fading away at the time when the yellow pigment is increasing These data are, of course, of an entirely different order than those obtained by the older methods and it is difficult to compare the two results But taking all observations, chemical and histochemical, into *consideration* it may be said that the possibility of a decrease of protein in old age is suggestive Probably cells do not diminish in size (23) On the other hand morphologic evidence discloses that all cortical layers show a diminution in cell numbers with age and such changes are in agreement with a decrease of protein (23 24) According to Brody and others, (23), *neuronophagia* is not limited to extreme old age but goes on throughout most of the life period Not only cell bodies (23, 24) but also the myelinated processes disappear (24a) Thus both intracellular neuronal materials and extracellular myelinated substances are depleted As previously discussed it seems logical that the extracellular water compartment enlarges in a compensatory manner We have mentioned a yellow pigment ...

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, When
... cells as well as the peripheral nervous system cells of dogs are stained by the periodic acid Schiff reagent three kinds of stained material are seen in the cytoplasm of the nerve cells glycogen, granular and non-granular substances Neither the granular nor the non granular stained portions are observed in dogs under 10 years of age while all animals over 12 years of age reveal these two substances both of which increase with age The non granular material reveals the histochemical reactions of mucopolysaccharide attached to a protein Thus it is assumed to be a mucoprotein The granular substance ...

... throughout the central nerv

TABLE III 8

Total protein in percentage of fresh tissue human brain in relation to age (from MacArthur and Doisy (16))

	Fetus		Infant			Adult			
	3 mo	7 mo	1 mo	3 mo	8 mo	21 yr	33 yr	35 yr	6 yr
Protein	3 77	3 98	4 57	5 29	6 09	8 03	8 11	8 99	7 53

TABLE III 9

Estimated protein content of cerebral gray and white matter per cent fresh tissue human brain in relation to age (calculated from data of Brante (17))

	Years					
	1	2 5	10-16	19 55	65 76	78-90
Gray matter						
No of brains	2	3	4	2	4	3
Estimated protein content	7 08	8 34	10 89	12 00	8 51	8 39
White matter						
No of brains	3	3	4	4	3	2
Estimated protein content	7 62	11 57	10 96	11 60	10 90	10 40

solvents, will include total acid soluble substances but since these are relatively constant (16) we may assume differences are due to fluctuations in protein[1] (table III 9) A steady increase of protein from one year to the 19 to 55 year period is observed both in gray and white matter, followed by a regression which occurs during the last two periods indicated in the chart Observations of proteins are of special interest since enzymes have protein moieties A diminution in protein may be associated with a lesser concentration of enzymes and some may grow while others decay For that reason the measurement of the protein does not give us information on direction of change in any specific enzyme Yet it is suggestive that proteins do decrease in old age at the same time that cerebral metabolic rate undergoes impairment [2]

Within recent years, new micromethods have been developed for the examination of protein within a single cell The study of the absorption spectrum of a single nerve cell area containing nucleic acid is some measure

[1] The values for protein are free of contamination with lipid nitrogen because that substance was extracted by lipid solvents They do however fail to include proteolipids which were extracted along with the lipids (20)

[2] Despite a decreased quantity of brain protein the quality remains relatively constant as indicated by the essentially unchanged amino acid composition (21)

of its protein content, for PNA (pentose nucleic acid) forms a pentose nucleoprotein The maintenance of normal neuronal function is associated with the production of pentose nucleoprotein and large amounts of that complex substance are found in the large nerve cell of the adult What is significant for the present study is that the amount of PNA decreases with old age (22) X ray microradiography reveals that the parts of the brain containing pentose nucleoprotein possesses much less dry matter than areas containing a yellow pigment a substance which accumulates in old age Thus the nucleoproteins are fading away at the time when the yellow pigment is increasing These data are of course, of an entirely different order than those obtained by the older methods and it is difficult to compare the two results But taking all observations chemical and histochemical, into consideration it may be said that the possibility of a decrease of protein in old age is suggest [illegible]

[illegible] crease of protein (23 24) According to Brody and others, (23), neuronophagia is not limited to extreme old age but goes on throughout [illegible]

[illegible] unsaturated substances are depleted As previously discussed it seems logical that the extracellular water compartment enlarges in a compensatory manner We have mentioned a yellow pigment or yellowish brown pigment which appears in the human central nervous system in increased amounts as the individual grows older Apparently its rate of destruction is slower than that of production This interesting sign of aging has been studied systematically in dogs from 2 to 17 years of age (25) When the central nervous system cells as well as the peripheral nervous system cells of dogs are stained by the periodic acid Schiff reagent, three kinds of stained material are seen in the cytoplasm of the nerve cells glycogen, granular and non granular substances Neither the granular nor the non granular stained portions are observed in dogs under 10 years of age, while all animals over 12 years of age reveal these two substances both of which increase with age The non granular material reveals the histochemical reactions of mucopolysaccharide attached to a protein Thus it is assumed to be a mucoprotein The granular substance [illegible]

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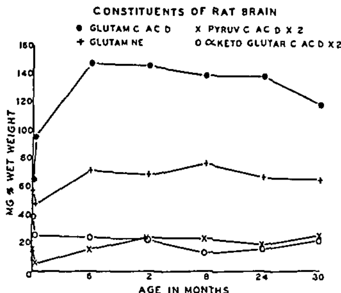


Fig III 2 Constituents (mg %) of rat brain from birth to 2½ years of age

ous system as life proceeds (22) It appears in the motor nerves motor root cells the pyramidal cells and in the sensory and sympathetic ganglia cells This yellow granular matter is present in large amounts in the cytoplasm of an increasing number of cells with aging It is not associated with any pathologic changes for the function of the central nervous system does not seem to be altered by its presence So far it appears to be simply one of the many signs of aging

Finally we should like to present some results obtained in our laboratory which have not been previously published (14) values for glutamic acid *glutamine pyruvic acid and alpha ketoglutaric acid of the brain through* out the life span of the rat including values up to two and a half years of age (fig III 2) We may observe in the first place that pyruvic acid and alpha ketoglutaric two *intermediaries of energy metabolism constantly* occurring in the brain reveal a fall in the first ten days of life after which there is a stabilization of their concentrations throughout the remainder of the life span Such a relative constancy indicates the continuous necessity for these reactions to maintain life Glutamine exhibits an early fall in contrast to glutamic acid which rises rapidly during postnatal life These substances attain maximal values during maturity glutamate earlier glut amine later and they reveal consistent decreases subsequently The reduced concentrations of these substances in old age do not prove that the brain is hydrated at this time but such changes are compatible with that possibility

In conclusion we may say that *the biochemical data for the brain in old* age is sparse Additional studies should be made using not only the well known chemical methods for the various solid constituents of the central

nervous system but also the newer histochemical techniques The results suggest diminished amounts of solids in the central nervous system, both in lipids and proteins in old age If this suggestion is sustained by further work then the decrease in protein is compatible with that of the cerebral metabolic rate observed in old age

The studies of the brain in fetuses and the newborn have revealed the rapid changes which take place at that time Quantitative studies made at later periods seem to disclose a more static condition And yet we know that this is only relatively so that there is a constant interchange going on so that if the total concentration of a brain constituent apparently remains the same it is simply due to the fact that the rate of production is approximately equalled by the rate of destruction. The observations made with the aid of absorption spectra support the results obtained by chemical measurements of the various constituents of the brain and yield added evidence that even in old age changes in these constituents are going on at a fairly rapid rate

In early life production gets ahead of destruction and growth occurs In extreme old age the reverse seems to be true as the solid parts decrease Change must be regarded as part of life

DISCUSSION

See Chapter IV

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CHAPTER IV

HUMAN CEREBRAL BLOOD FLOW AND OXYGEN CONSUMPTION AS RELATED TO AGING[1]

SEYMOUR S KETY

The circulatory nutrition of the brain is one of the fundamental components upon which are built the more subtle, more complex and less accessible frameworks of function Over the past decade, a number of investigators have elicited information on the over all circulation and oxygen consumption of the human brain at various ages over practically the entire life span It seems apporpriate to review these data, to observe whatever consistency or correlations appear, and to begin to form hypotheses to be tested in future work

These investigators have used the nitrous oxide technique (1), which yields an average value of blood flow per minute for unit weight for the brain as a whole, from which are derived similar units of oxygen consump

[illegible] employed a later modification (3) of this technique in wh[illegible]

[illegible] are not always available, an attempt at correction of such data can be made from a comparison of values obtained in the range from 20 to 30 years of age where the results of other groups have been quite consistent A correction factor of 0 85 thus obtained has been applied to their data in figures IV 1 to IV 3 The precise value of this correction or, indeed whether it is necessary at all is somewhat irrelevant to the present argument since the data in question show the same relative trend with age as do the others

In an effort to restrict the relevance to the normal processes of maturation and aging some pains have been taken to include all of the series where age rather than disease was the primary [illegible]

[illegible] tutes of Mental Health and Neurological Diseases and Blindness National Institutes of Health Public Health Service Department of Health Education and Welfare Bethesda Md.

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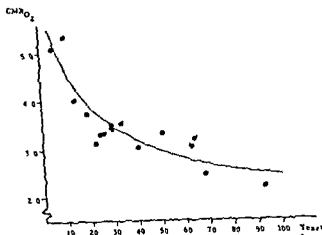


Fig II 3 The relationship between cerebral oxygen consumption (ml per 100 g per min) and age in years

TABLE IV 1

Data and sources

Authors	Ref	No Cases	Mean Age	CBF*	CMR_{O_2}*	CVR*	$(A-V)_{O_2}$*
Kennedy *et al*	(6)	6	5	104	5.1	0.8	4.8
Kennedy *et al*	(7)	7	10	90	5.3	0.9	6.2
Kennedy *et al*	(ı)	7	13	68	4.0	1.1	6.0
Sokoloff *et al*	(8, 9)	4	19	60	3.70	1.5	6.2
Sokoloff *et al*	(8, 9)	7	23	52	3.12	1.8	6.3
Kety and Schmidt	(1)	14	25	54	3.3	1.6	6.3
Scheinberg and Stead	(3)	19	25	65†	3.8†	1.3†	6.0
Schieve and Wilson	(4)	12	29	62†	4.0†		6.6
Shenkin et al	(10)	12	30	53	3.4	1.8	6.6
Fazekas *et al*	(11)	9	34	51	3.5	2.1	6.5
Schieve and Wilson	(4)	10	40	57†	3.5†		6.4
Scheinberg *et al*	(2)	16	50	59†	3.8†	1.6†	6.4
Scheinberg *et al*	(2)	16	63	51†	3.4†	2.0†	6.7
Schieve and Wilson	(4)	7	64	55†	3.7†		6.7
Fazekas *et al*	(11)	15	68	43	2.4	2.9	5.5
Fazekas *et al*	(12)	18	93	39	2.3	2.7	5.8‡

* CBF represents cerebral blood flow (ml per 100 g per min) CM_{O_2} represents cerebral oxygen consumption (ml per 100 g per min) CVR represents cerebrovascular resistance (mm Hg per ml per 100 g per min) $(A-V)_{O_2}$ represents cerebral arteriovenous oxygen difference (vol per cent)

† Data may incorporate a systematic error which raises CBF and CMR_{O_2} and lowers CVR respectively all by about 15 per cent The adjusted values have been used in figures IV 1 to IV 3

‡ Calculated from CBF and CMR_{O_2}

approximation to the normal aging process since practically all represent hospitalized patients, even though their diseases were unlikely to affect the cerebral circulation The sources of these data, the mean age and number of cases in each series, are given in table IV 1 Each report usually contained sufficient information to indicate that the values obtained would be representative of normal values In five of the series the subjects were apparently normal, non hospitalized individuals (1, 3, 6, 8, 9) Some consisted of alert and active patients with no cardiovascular disease, hospitalized for minor elective surgery (2) or for minor illness (1) Some groups recorded the absence of cardiovascular (2, 4, 10, 11) and neurologic disease (2 4, 11) The

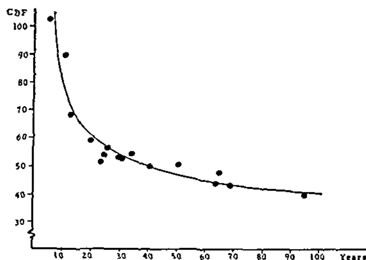


Fig II 1 The relationship between cerebral blood flow (ml per 100 g per min) and age in years

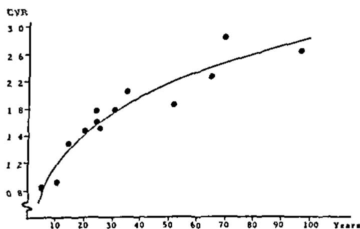


Fig II 2 The relationship between cerebral vascular resistance (mm Hg per ml per 100 g per min) and age in years

mixing of cerebral venous drainage even if it occurred with advancing age would not be a systematic one but could reflect itself only in a greater scatter of the individual data On the other hand a progressive increase in contamination of internal jugular blood with blood from the less well perfused and more slowly metabolizing extracerebral tissues could produce some of the changes observed Since in the adult this contamination is less than 3 per cent it could certainly not account for the dramatic changes observed during adolescence Furthermore the nitrous oxide technique as originally described offers a means of detecting the presence of at least gross contamination In two studies on elderly individuals performed by the original technique (10 18) there was no evidence to suggest the presence in such patients of a degree of contamination significantly greater than that which obtains in normal young men All of these considerations although admittedly indirect speak against the possibility that the age correlation of cerebral blood flow and the other related functions is the result of an anatomic artifact

Since there is evidence (19) to suggest that certain types of anxiety may be associated with significant increases in cerebral oxygen consumption and blood flow it is important to consider the possibility that the un[illegible]

[illegible] recognized this possibility and took considerable pains to minimize it These included the use of a plastic space dome instead of a face mask projection of animated cartoons during the procedure and refusal to continue the studies at the first sign of uncooperativeness In the opinion of this reviewer anxiety was held to a minimum by this group as well as the others and in any case was not likely to show an age dependent variability

There is good reason to believe therefore that the values summarized for the various functions are a close approximation to [illegible]

[illegible] technique yields results only in terms of unit volume or (since its specific gravity is quite constant) unit weight of brain It does not distinguish between cellular and extracellular active or metabolically sluggish masses The change [illegible]

[illegible] of the brain as a whole Although a decrease in neuronal density is commonly regarded as a concomitant of advancing age the author is aware of only one quantitative

two older series of Kennedy (7) consisted almost entirely of children under study because of a previous history of mild convulsive seizures in no case had there been a seizure within several days of the procedure and none of the patients were receiving any drug therapy Previous work in adults (13) had demonstrated no abnormalities in the functions under consideration in such patients Schieve and Wilson (4) included a few schizophrenic patients in two of their series but again a previous study (14) had shown no change from normal in cerebral hemodynamics or metabolism in this disease In the oldest group (12) only one third of the subjects were mentally alert the remainder showing various degrees of deterioration the mean values for the six mentally normal individuals however were the same as those for the series as a whole

REVIEW OF RESULTS

The relationship between age and cerebral blood flow is presented in figure IV 1 Each point represents the mean of a series of determinations During the first decade of life the values for both cerebral blood flow and cerebral oxygen consumption are quite high the latter representing 48 per cent of the total oxygen consumption of the child in the basal state There appears to be a rapid fall in the over all cerebral circulation about the time of puberty which continues through adolescence From the third decade onward there is a more gradual but continuous decline in this function through middle and old age Figure IV 2 depicts a similar but reciprocal change in cerebrovascular resistance a function which represents the sum of all of the factors which hinder the flow of blood through the brain The changes in cerebral oxygen consumption expressed as ml of oxygen utilized per 100 g of brain per minute are given in figure IV 3 This shows similarly a rapid and then more gradual fall with advancing years

These findings for cerebral blood flow oxygen consumption and cerebrovascular resistance seem quite clear cut and considering the large number of individual investigators involved the data show relatively little scatter Their interpretation however is not so definitive One must first entertain the possibility that these changes are the result of some age dependent artifact The values obtained by use of the nitrous oxide technique apply rigorously only to the tissues and regions which are represented in the blood at the superior bulb of one internal jugular vein There is satisfactory evidence (1) that in most individuals such blood is representative of blood in both internal jugular veins and is only insignificantly (less than 3 per cent) contaminated with blood arising from extracerebral sources (17) There is practically no evidence however that these sources of error demonstrably negligible in a general sample of the population show no progressive increase with age *The effect of progressively poorer*

mixing of cerebral venous drainage, even if it occurred with advancing age, would not be a systematic one but could reflect itself only in a greater scatter of the individual data On the other hand, a progressive increase in contamination of internal jugular blood with blood from the less well perfused and more slowly metabolizing extracerebral tissues could produce some of the changes observed Since in the adult this contamination is less than 3 per cent it could certainly not account for the dramatic changes observed during adolescence Furthermore, the nitrous oxide technique, as originally described, offers a means of detecting the presence of at least gross contamination In two studies on elderly individuals performed by the original technique (10 18), there was no evidence to suggest the presence in such patients of a degree of contamination significantly greater than that which obtains in normal young men All of these considerations although admittedly indirect, speak against the possibility that the age correlation of cerebral blood flow and the other related functions is the result of an anatomic artifact

Since there is evidence (19) to suggest that certain types of anxiety may be associated with significant increases in cerebral oxygen consumption and blood flow it is important to consider the possibility that the unusually high values for these functions found by Kennedy and his colleagues in childhood were the result of a decreased acceptance of the procedure and a greater apprehensiveness on the part of these subjects It is apparent that these investigators recognized this possibility and took considerable pains to minimize it. These included the use of a plastic space dome' instead of a face mask projection of animated cartoons [illegible]

[illegible] in any case, was not likely to show an age dependent variability

There is good reason to believe, therefore, that the values summarized for the various functions are a close approximation to those which exist in the normal resting state at various ages One may formulate a number of hypotheses in an attempt to explain the changes which occur in association with age The nitrous oxide technique yields results only in terms of unit volume or (since its specific gravity is quite constant) unit weight of brain It does not distinguish between cellular and extracellular, active or metabolically sluggish masses The changes therefore, could be a reflection of a generalized decrease in the circulation to and metabolism of the individual actively metabolizing units or equally well a progressive reduction in the ratio of their mass to that of the brain as a whole Although a decrease in neuronal density is commonly regarded as a concomitant of advancing age the author is aware of only one quantitative

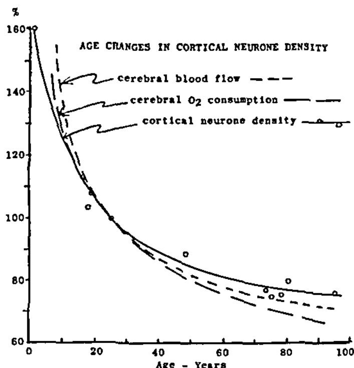


Fig IV 1 Mean values for neurone density in four areas of cortex at different ages from data of Brody (20) The mean age curves for cerebral blood flow and oxygen consumption are included for comparison All values are expressed as per cent of the respective mean value at age 25

study on the human brain (20) Although this study was restricted to neuronal density in certain areas of the cerebral cortex and may not have controlled completely such artifacts as shrinkage, it is hardly likely that these could have accounted for more than a small share of the marked decrease in the average neuronal population which was found to be associated with age The striking similarity between this curve (fig IV 1) and the curves for cerebral blood flow and oxygen consumption suggests more than a chance relationship

Regardless of whether one or the other or both processes are occurring in association with maturation and aging, some more fundamental and age related causes must be sought capable of affecting the metabolic activity or the survival of the active components These findings are compatible with at least two hypotheses The more obvious and, until recently, the generally accepted one would attribute to the circulation a primary role with metabolic and functional changes the result of alterations in the cerebral blood supply There is no evidence that under normal circumstances an augmentation of the circulation to the brain will produce

an increase in its metabolism and, therefore, little reason to attribute the high cerebral oxygen consumption found by Kennedy in childhood merely to the increased circulatory rate On the other hand, the undeniable postulate that oxygen consumption must at some point be limited by oxygen delivery makes at least tenable the hypothesis that the decreased functional acuity of the aging brain is dependent upon its slowing rate of metabolism which is, in turn the result of the progressive diminution in circulation The common, if not invariable, finding of some degree of cerebral arteriosclerosis associated with old age, perhaps reflected in the progressive increase in cerebral vascular resistance, supports this hypothesis and, in fact, provides a reasonable mechanism for the circulatory deficit

Failure to find a significant correlation between loss of mental acuity and generalized cerebral circulatory or metabolic deficit (11) does not invalidate this hypothesis since cerebral as well as general arteriosclerosis is known to be unevenly distributed, while mental acuity is so poorly localized a function as to require the destruction of a large portion of the brain before an impairment is detectible An observation less readily reconciled with the hypothesis is the fact that there is not found a significant decrease in cerebral oxygen consumption in acutely induced anoxia (21) or hypotension (22 23) of sufficient severity to affect the mental state quite perceptibly It is possible to argue, of course, that the circulatory deficit in aging is hardly an acute process and that metabolic sequelae may occur after many years which are not apparent within a few minutes

More important than the soundness of the arguments against the hypothesis of primary cerebral circulatory deficit, however, is the absence of crucial evidence in its favor and at least one alternative hypothesis must be entertained This would postulate that a more fundamental cerebral derangement in aging lies in the diminished metabolic demands of the brain This could be the result of simple loss of neurons which had fulfilled their life spans a progressive deterioration in certain essential cellular components, a decrease in neuronal interconnections and interaction or a lessened functional demand as a result of the psychological and social changes which attend the aging process Whatever the cause of such reduced requirements and those listed are hardly a complete tabulation the restricted cerebral circulation and increased vascular resistance could follow rather than cause the decreased metabolism Whether achieved by the vasodilator effects of the products of metabolism or by some local reflex an adjustment of the circulation to meet metabolic demand is reasonably well established in the brain as well as in other tissues Such an hypothesis of functional and metabolic aging of the brain, in

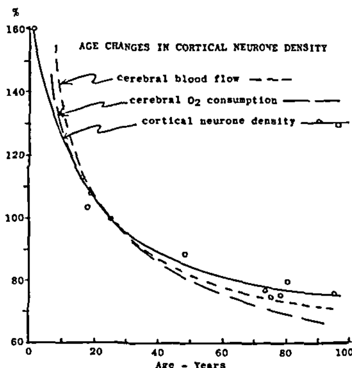


Fig IV 4 Mean values for neurone density in four areas of cortex at different ages from data of Brody (20) The mean age curves for cerebral blood flow and oxygen consumption are included for comparison All values are expressed as per cent of the respective mean value at age 2[illegible]

study on the human brain (20) Although this study was restricted to neuronal density in certain areas of the cerebral cortex and may not have controlled completely such artifacts as shrinkage it is hardly likely that these could have accounted for more than a small share of the marked decrease in the average neuronal population which was found to be associated with age The striking similarity between this curve (fig IV 4) and the curves for cerebral blood flow and oxygen consumption suggests more than a chance relationship

Regardless of whether one or the other or both processes are occurring in association with maturation and aging some more fundamental and age related causes must be sought capable of affecting the metabolic activity or the survival of the active components These findings are compatible with at least two hypotheses The more obvious and until recently the generally accepted one would attribute to the circulation a primary role with metabolic and functional changes the result of alterations in the cerebral blood supply There is no evidence that under normal circumstances an augmentation of the circulation to the brain will produce

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dependent of circulatory supply, is supported by the occurrence of some *type of age associated functional deterioration in certain species like the* rat which do not develop arteriosclerosis

The distinction between a primary circulatory and a primary metabolic or functional deficiency in the aging brain, although of considerable pertinence to an understanding of senility and to rational attempts to retard or ameliorate it, cannot be made definitively on the basis of present data A possibility is presented, however, of obtaining some indication of the real sequence of events by means of the cerebral arteriovenous oxygen difference This quantity can readily be shown to vary inversely with the ratio of cerebral blood flow to cerebral oxygen consumption so that this measurement, although conveying no information with respect to either blood flow or metabolism separately, is an accurate measure of the relationship between them In all cases where there is a primary reduction in cerebral circulation, such as hyperventilation (21) or an acute fall in blood pressure (22, 23) there is a significant increase in cerebral arteriovenous oxygen difference while this value is consistently low in those states such as anesthesia (24) diabetic (25) or insulin coma (14) where the primary depression is clearly in cerebral oxygen demand Unfortunately, the behavior of the cerebral arteriovenous oxygen difference in senescence is equivocal (fig IV 5) Although the data as a whole show a tendency toward a widening of this arteriovenous difference suggesting a greater circulatory than metabolic involvement two of the series are

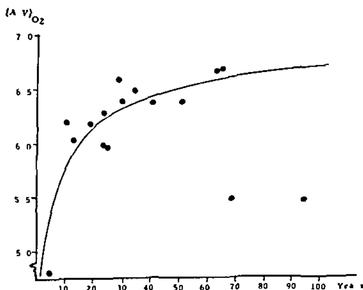


Fig II 5 The relationship between cerebral arteriovenous oxygen difference (ml per 100 ml) and age in years

markedly aberrant It is quite possible that a primary circulatory deficit may if sufficiently severe and chronic, produce intracellular changes resulting in an overriding decrease in metabolism and thus obscure the analysis in later stages of the process This factor, in addition to the presence of severe anemia, which also causes *per se* a reduction in the cerebral arteriovenous oxygen difference probably contributed to the ambiguity of some of the measurements reported This concept however, if applied to more carefully selected subjects may provide a greater insight into the dynamics of aging in the brain

SUMMARY

A review of available information on over all cerebral blood flow and oxygen consumption in man obtained by means of the nitrous oxide technique reveals a distinct correlation of these functions with age

There is a rapid fall in the circulation and oxygen utilization of the brain from childhood through adolescence followed by a more gradual but progressive reduction throughout the remaining age span

The factors responsible for these changes and whether one or the other is primary appear to be suitable subjects for continued investigation

DISCUSSION

DR H HOUSTON MERRITT [New York N Y] It was a great privilege to read these two papers and to hear them presented by men who have done so much work in this field

You will all perhaps recall that it was Dr Kety working with Dr Schmidt, who devised the method for studying cerebral blood flow with nitrous oxide and Dr Himwich has spent a lifetime studying bra n chemistry

Dr Kety has collected all the data of the literature which deal with the cerebral circulat on and has arranged the results according to age

Kety tried to rule out all artifacts

with specific changes in metab

that even in elderly individ

active one

because it would seem to me

Barcroft in 1914 made a statement which was of such great significance that it has now become known as Barcroft s law there is no instance in which it can be proved that an organ increases its activity under physiological conditions without also increasing its call for oxygen The reverse of that would seem to apply in old age With decreased physiological activity there is a decrease in the call for oxygen and a decrease in cerebral blood flow If we accept this hypothesis it can be assumed that the reduced call for oxygen is related to reduction in the functional activity of the brain

On that basis then we could say that probably, there are two causes for this reduced activity of the brain One is a relative reduction in proportion of the functional units and the other a reduction of the metabolism of the functional units that persist Dr Himwich and Dr Kety both show that there is a reduction in the cerebral functioning units with age Dr Kety s Figure IV 4 showed that the reduction in oxygen consumption and reduction in blood flow exactly paralleled the cell population It should not be assumed however that the cell body is the sole seat of function of activity in the neuron and that a reduction in the cell population is the main factor in oxygen utilization The myelin sheaths of the axon constitute a substantial portion of the mass of the nervous tissue and recently Lowry and his coworkers have suggested that on the basis of differences in enzymatic content of heavily myelinated and lightly myelinated layers of the cortex myelin itself has an active metabolism

Changes in lipid may reflect the decrease in myelin with age Presumably this decrease is a result of change in the protein moiety of the myelin sheath Thus it may be that the reduction in myelin may be an important factor in the reduction of cerebral metabolism and may play a role independent of cell loss because myelin can degenerate without cell loss

If it is granted that reduction in functioning metabolic units is a normal accompaniment of aging it is interesting to speculate why decrease in mental facilities is much more severe in some individuals than in others Pathological processes may be the explanation of some cases In others we can only postulate that there may be a variation in the rate of degeneration of specific cortical areas in different individuals As both authors have pointed out a great deal more work needs to be done and studies should be made in connection with psychological studies of the individuals in order to reach some conclusion in this regard

Dr Nathan W Shock [Baltimore Md] I had not anticipated being called upon to make any remarks at this time but I do think that the points made by Dr Kety highlight the necessity for making some distinction between what is going on in the cells that remain in the aging organism and the effects of loss of functioning cells or units

I do not know to what extent the reported reduction in the number of neurons and cellular elements in the nervous system with age determines changes in performance However we do have a very large body of information indicating that as the organism ages there is a gradual diminution in the number of functional elements To me this represents one of the major problems we must face in studying aging animals because after all one of our primary interests is to explain any age reduction in performance To do this we must be able to distinguish between alterations in cellular functions and the loss of cells

I think that the earlier papers which indicated a necessity for processes of repair for the cellular elements of the nervous system apply equally well to any tissue of the body What we really want to know is what the physiological characteristics are that cause a particular cell in a particular organ to lose its ability to maintain its own integrity Is this a question of a purely statistical chance affair? Is it cosmic radiations that cause the

dropping out of a specific cell at a specific time, or, as Dr Lansing has implied, is there some built in process that operates at varying rates within cells that causes them to lose this restorative capacity?

DR WILLIAM MALAMUD [Boston, Mass] I have two questions I want to ask—that is, provided these questions are really going to be answered and will not be simply rhetorical questions

Dr Kety intrigued my curiosity very much in his preface when he spoke about the fact that in trying to understand the processes of aging, it is essential not to restrict oneself to the brain or the central nervous system, but also extend one's investigation to the other organs of the body, and even to social and psychological factors dependent upon interrelationships with other persons

Somehow he did not get around to talking about the second part of it, and I wonder whether he could elaborate a little on how social and psychological stress, aside from the one thing he mentioned, namely, anxiety, may have an effect (as I am sure they must have) upon brain circulation

The other question I wanted to ask is in relation to a previous paper We were encouraged not to ask questions of the first two speakers because of the fact that it was suggested and quite justifiably, I think, that we didn t know very much about their subject. However, I think that that is really an argument for our asking questions rather th...

... of France a id a number of other people, it was shown that the spinal meningeal permeability, and also the blood brain barrier actually increase with vascular diseases such as arteriosclerosis and general paresis, etc. He referred particularly to vascular diseases

The other point is—and I see Dr Welch sitting right across from me here—that he spoke about the fact that the highest degree of permeability is found in embryos, and that the greatest decrease in permeability occurs very early in life rather than late I may be misquoting Dr Welch If I am, he may want to talk about it

DR. RALPH GERARD [Ann Arbor, Mich] Since visual impressions are so much more weighty than auditory ones, and a curve carries such weight, I would simply like to call to the attention of the audience explicitly what was clearl...

... [illegible] was, as I estimated it, something like 20 per cent—say an average of 5 per cent per decade

It is also worth rememb... oxygen consumption ar... very early years of life... the functioning of the... way questioning... them—it is health... in these brain at... of diminution often great, in function ... that is unequivocally the basis

PRESIDENT MOORE Dr Weiss do you care to discuss these papers? Perhaps, at the same time, you might answer Dr Malamud.

DR PAUL WEISS [New York N Y] I can t answer these questions but I should like to call attention to the direction in which our biological thinking is turning in answering such questions

We used to think in terms of single causes We asked whether the cause of this or that change lies in the nucleus or in the pigment or in metabolism or in oxygen con sumption whether it acts from the outside or from within, whether it is genetic or hormonal or nutritional or social or what not Now, one thing is becoming clear We can no longer consider any one part of an organic system in isolation All these parts are interrelated As a mere generality such a statement has little practical meaning but we are beginning to learn about the precise manner in which they interdepend

Now, if we remember that in a machine the different types of gears the lubricants the fuel supply etc are all interdependent and essential for its operation within a given latitude called tolerance we realize that any group of events that will strain these interrelations beyond the limit of tolerance will cause its eventual disruption What this means in terms of the questions that have been asked regarding the organism is this All cells all systems of the body are constantly bombarded one might say by incidents by the variations the unpredictable contingencies of the life they lead within a variable environment—the nucleus within the cellular environment the cell in the tissue the tissue in the community of organs the organism in the community in which it lives These variations are random in their directions and varied in their parameters With regard to any single parameter you will find that some of these variations have a positive sign and others have a negative sign so that statistically they will frequently cancel out

However if any number of these slight accidents which we call variability pile up in the same sense and build up residues then you finally find a state where the normal coordinating and regulating capacities of that interrelated machinery will no longer work It will exceed the limit of tolerance that has been built into the machine as the stress limit within which it can still operate and once that is reached then you are faced with a failure of the machine

So what is happening then is a breakdown of *relations* of interrelations which have to be intergeared with one another mutually supporting each other in order that the whole system can function Just how this strain will build up in each case depends on a great many accidents which vary from place to place in the system from particle to particle all the way up to the particles that form communities

In all those cases I maintain that it is quite possible to find the tangible instruments the actual points at which the incongruities develop Therefore if social factors were introduced I doubt whether there is any way in which they can become effective except through the agency of individuals and the individuals through the agency of their brains and their tissues and these tissues through the agency of their cells and the cells through their components Therefore they are open to analysis and this is for the future to do rather than to look for and enter into ideological warfare about single causes whether it be in the case of cancer or in the case of aging

This is a rather general answer but I believe it bears on the question that has been asked

PRESIDENT MOORE Are there any further questions for Dr Kety or Dr Himwich from the members of the Commission? If not there is a question submitted by Dr R I Mackay Chicago Would Dr Kety agree that the nonvascular nature of the histopatho logical changes in Alzheimer s disease—fibrillar intracellular changes and plaques—as well as in other cases of senility suggests that the processes of senility are basically intra cellular and biochemical rather than vascular?

DR. SEYMOUR KETY I want to thank the discussers for their comments In regard to Dr Weiss s comment I do not always find it easy to accept *a priori* that every biological phenomenon is caused by a multitude of important factors in fact one of the reasons for studying the cerebral circulation in aging is to rule out the possibility that a single factor is operating

If an automobile manufacturer were to produce automobiles which for some reason had a poorly designed fuel line which after ten or twenty thousand miles became impacted with some kind of sediment it would be very easy to suppose that the machine could break down and age as a result of this very simple single phenomenon which could possibly be corrected. In the same way there has been the hypothesis that mental aging is the result of a sclerotic fuel line and some of these observations were made to test this rather simplified assumption I think that the conclusions would bear out Dr Weiss s postulate that things are not quite that simple

With regard to Dr Gerard s question I think that the explanation for that lies in the fact that I inherently dislike empty space and to have plotted these with zero appropriately placed upon the ordinate would have wasted an extravagant amount of space As he mentioned however there was clearly indicated the relationship of these data to the zero po n

... will produce what functional change in the nerve cell

With regard to the question about Alzheimer s disease I would invoke my inherent *faith that* the relevant answers to most of these problems are probably going to be in the metabolism and in the biochemistry rather than in the plumbing of the brain and I would certainly agree with the individual who made that point

In answering to Dr Malamud s interesting question I might say that it was not my purpose nor did it lie in my field of competence to elaborate upon the mechanisms by which sociological and *psychological* changes may affect nervous and mental function However I have no doubt that such mechanisms do exist and someone some day may be able to demonstrate them

We do know that in the case of anesthesia for example where there is a profound reduction in the oxygen consumption of the brain this can not be attributed to a direct interference with oxidative metabolism *by the anesthetic* but according to more recent concepts it involves the interruption of synaptic transmission as the primary effect of the anesthetic following that interference with f n

tell

po n

DR. HAROLD HIMWICH One of the questions still unresolved is the cause of the decreased cerebral metabolic rate of old age Where vascular changes are predominant it is tempting to conclude that they are primary and

... poi t concurred in by Dr Merritt ... still a diminished oxygen re-

It is also worthy of note that in old age the cerebral metabolic rate is impaired

whether or not the patient is apparently normal or psychotic or exhibits neurological signs As Dr Kety remarked his method gives the oxygen consumption per 100 grams of brain per minute It is an overall result and does not necessarily yield information on any particular part of the brain The area of the brain damaged however will de termine whether or not there are symptoms If a so called silent area is destroyed altera tions will not be observed If a strategic structure is attacked however the patient will exhibit behavioral changes

Our review of the literature indicates a decrease in the various constituents of the brain The diminished cerebral metabolic rate of old age may be due either to an im paired oxygen consumption of all brain cells or to a decreased number of cells The second of these two viewpoints namely that cells have been destroyed by one process or another suggests that all healthy cells retain a fairly constant metabolic rate not only in mature life but throughout the senium The reduction in oxygen consumption would then be a reflexion of the decreased number of surviving cells

Finally I want to thank Dr Merritt for his fine discussion and especially for bring ng out parts of my paper which time limitations did not permit me to present in my discus sion

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CHAPTER V

AGING AND INTELLIGENCE

IRVING LORGE

At the end of World War I the War Department released the Army Examination Alpha for use in the testing of intelligence of civilians To date the most elaborate application of Alpha was made by Jones and Conrad in their appraisal of the mental ability of the total population in the age range of 10 to 60 years in nineteen New England villages On the basis of about 1200 tests they concluded that the developmental curve for *the total Alpha test may be summarized as involving a linear growth to* about 16 years with a negative acceleration beyond 16 to a peak between the ages of 18 and 21 A decline follows which is much more gradual than the curve of growth but which by the age 55 involves a recession to the 14 year level (1)

This interpretation of their results is responsible for the generalization that intelligence declines from its maximum at or near early maturity *i e in the twenties It is my* contention that their interpretation was an overgeneralization when it was made and that today the results would not demonstrate so dramatic a decline

Let us look at the Army Alpha itself Under the pressure of military need the Army Alpha was developed as a test to be given to groups of soldiers In general it was based primarily upon the philosophy and methods involved in the origination of the Binet-Simon Scale and the Terman revision of it *It* was fortunate indeed that *Arthur S Otis had* progressed in the making of his Point Scale sufficiently so that it could be adapted quickly for the making of Alpha The Binet-Simon Scale and all subsequent adaptions of it arrive at an estimate of a child s—or of an adult s—mental endowment through the presentation of a wide range of tasks differing in content in processes and in the demands for speed and/or accuracy The criterion that Binet was trying to estimate was *school adjustment the performances on the tasks should be related to* success in learning the facts skills and generalizations taught in school In general Binet and Simon assumed that the brighter the child seemed to his teacher in school the greater would be the number of facts skills and ideas he would have acquired and hence the greater his capacity to learn more such facts skills and ideas in his subsequent education Thus Binet and Simon estimated ability to learn in school via the amount of *learning* that had already been accomplished The Binet-Simon Scale

thus included a wide range of tasks that required knowledge of the child's environment. The test questions are a broad mixture of items about word knowledge, arithmetic reasoning, and verbal comprehension, as well as tasks which required fine discriminations, immediate and delayed memory, and the ability to make inferences and generalizations.

The Army Alpha, based as it is upon the Binet-Simon Scale, was built in eight subtests representing a wide range of content and of process. The eight subtests were: Oral Directions, Arithmetic Problems, Practical Judgment, Synonym-Antonym, Disarranged Sentences, Number Series Completions, Analogies, and General Information. Each subtest gave credit for speed in performing tasks. The time limits varied from five seconds for a single item in the Oral Directions subtest to five minutes for the entire subtest of Arithmetic Problems.

The evidence is clear that neither the Binet nor any of its successors (such as Army Alpha, the Otis Self-Administering Test of Mental Ability, the Army General Classification Test—AGCT—of World War II, or the recently published Wechsler Adult Intelligence Scale) do measure a single or unitary component of intellectuality. By design, each of these intelligence tests measures an undifferentiated mixture of content, process, and speed. The factor analysts have identified more or less adequately over forty different but correlated components in intelligence tests. Thurstone, for example, has identified at least seven major factors or components relating broadly to content, process, and speed. His content factors were named space, number, verbal comprehension, and word fluency; the process factors are called associative memory, perceptual speed, and reasoning. Of course, in a sense, the factor analyst finds in intelligence tests what the test maker had incorporated *into the* test. For the most part, current intelligence tests emphasize those processes and contents deemed significant for predicting the amount and kind of learning in the school subjects at all levels from the primary grades to post-graduate university education. Some critics of current intelligence tests may assert that the school learnings that are favored are like those considered important in the curricula from the 1890's to the 1920's. The narrow scope of most intelligence tests, therefore, did not, nor does not, give enough credit to broader objectives of social competence or social intelligence. The ability to get along with people, to empathize or understand them, may be as intellectual as the ability *to solve* a puzzle or to interpret a printed passage. Certainly no intelligence test designed for appraising the mental ability of adults has as its criterion the successful solution of the range of tasks adult life affords, such as meeting the intellectual requirements of vocation, family life, and economic and social adjustment. The criterion of mental ability needs to be extended to the successful handling of tasks

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must follow that the older members of the population necessarily are at some disadvantage not only because of their remoteness from formal schooling but also because they had less of it

Read Tuddenham has obtained some evidence about the value of formal schooling for intelligence test scores During World War II, he administered a version of Army Alpha to a representative sample of white enlisted soldiers The World War II soldiers made a median Alpha score of 104 whereas the median for the World War I draftee was 62 Dramatically the median for the 1940-45 soldiers was at the 88th centile of the 1917-18 distribution Of course World War II soldiers were probably more familiar with objective testing the tests were given by better trained examiners and examining conditions were controlled more adequately The difference however was due primarily to the amount of education the two generations of soldiers had received The World War II troops had a mean of 10 0 years of formal schooling whereas World War I s soldiers averaged 8 0 years Tuddenham interprets the results as indicating that the present population is superior in mental test performance to the population of a generation ago and that a large proportion of this superiority is a consequence of more and better education for more people (14)

How much education a person received depended on when he was born The census returns for 1950 indicate that the median for years of schooling completed for all persons in the age range 25 to 29 years was 12 1 in the age range 30 to 34 years it was 11 6 in the age range 35 to 44 years it was 10 2 in the age range 45 to 54 years it was 8 8 in the age range 55 to 64 years it was 8 4 and —

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in an [illegible] about intellectual decline which has less to do with mental ability as such than with the diminished educational opportunities afforded the older people in their childhood and youth

This possibility that schooling may be reflected in intelligence tests raises a major criticism of the kind of evidence utilized in so-called intellectual decline Jones and Conrad tested in their villages all persons aged 10 to 60 years They computed the average test performance by single years or by semi-decades on the assumption that all individuals in any one age group were just like those in any other age category The reported data on years of schooling completed demonstrates that for one variable at least the assumption is not justified Indeed it was less justifiable for the 1900 s than for the 1920 s and [illegible]

other than those represented by school tasks Intelligence tests in the last analysis represent the orientations of the test maker

It is not surprising that out of school adults make uneven performances on the eight different subtests of Army Alpha They are uneven because intelligence is not a single unitary factor they are uneven because the tests themselves do not evaluate adequately the full range of competences needed for successful adult activities Jones and Conrad found considerable differences among the eight subtests They reported that In some tests the adolescents are superior to most of the adults in others the adults on the average surpass the adolescents In some tests the peak of development is reached around 18 years in others a slight rise continues well into advanced maturity It is noteworthy that the tests of information (Test 4 opposites or vocabulary and Test 8 general information) fail to exhibit a post adolescent decline Decline is most rapid in Subtests 7 (analogies) 3 (common sense) and 6 (numerical completions) (4) In specifying the differential successes of adults on the various subtests Jones and Conrad add the interpretation that the three tests on which declines are *greatest may perhaps be considered* at least on *a priori* grounds to be the best in the Alpha for the measurement of basic intelligence or intellectual capacity (4) Jones at least has been steadfast in his belief that the two tests on which adults show no loss are the least valid for he said recently that the two tests (vocabulary and general information) can be shown to be less valid for age comparisons (9 p 271) There can be little doubt that Tests 4 and 8 more than some of the other subtests are measures of stored knowledge which most adults constantly use Stored knowledge of course does not remain static or unchanged in adults it is always being added to and subtracted from Remoteness from schooling disuse of content or process shift in emphasis to accuracy or even the adaptation of a way of working may influence test results Disuse of arithmetic reasoning or an overemphasis upon correctness of numerical completions may be responsible in part for some *of the lower scores in those tests by people in the later ages*

Basically the Army Alpha (and tests like it) must be and is correlated with the amount and quality of formal education In World War I the correlation between Alpha and the highest school grade reached for the native born white draftee was 65 In World War II the correlation between AGCT and highest school grade reached also was about 65 Schooling makes for a difference in intelligence test scores The greater the amount of schooling the higher the intelligence test performance It is well known that the older adults in the population have had much less formal schooling *than those persons born in the last 20 years Since there* is a positive correlation between schooling and intelligence test score it

made greater gains on the second test than their boyhood intellectual peers who had ceased their formal schooling sooner (7)

The most important follow up study however, was that made by Owens During 1949–50 he retested 127 men with the same form of the Army Alpha which they had taken as an entrance examination for Iowa State College in 1919 With great care he shows that the sample retested in 1919 could be considered representative of the entire 1919 *applicant group* Over the 30 year period the same individuals made a significant increment in the total Alpha score The over all gain was accomplished by significant increases in the subtests of Practical Judgment Synonym Antonym Disarranged Sentences Information and Analogies No subtest produced a

greater the probability of a gain on the retest Owens proposed a hypothesis that must ultimately be evaluated that individuals may have increased their scores on Army Alpha from the freshman to the senior year and that thereafter possible losses from their senior status occurred between age 20 and age 50 Even were the hypothesis to be verified it would suggest at the worst a very slow decrement in intelligence test score to the fifties

Bayley and Oden too retested a superior group over an extended period They readministered the Terman Concept Mastery Test (consisting of verbal items synonym antonym and verbal analogies) at or near age 41½ years to gifted adults who had taken the same test 12 years earlier They also obtained test and retest scores for the spouses of the gifted for the same time span For both *groups* scores were consistently higher at the second testing with somewhat larger gains on the synonym antonym subtest The Concept Mastery scores are positively related to the amount of education the respondents had had (1)

The Owens and the Bayley Oden follow up studies are based on select populations of former college students and of previously identified gifted persons (It is assumed that the spouses of the gifted are also select by assortative mating) The Lorge sample was just above the average of the population since the majority had achieved eighth-grade graduation in 1919 Birren would argue that the *rate* of intellectual change with age in the elite 5 per cent of the population would be quite different from the rest of the population (2)

Unfortunately not much evidence is

Obviously, results from cross sectional testing can allow inferences only about age differences, not about age changes Age changes can be appraised only by follow up retesting of the same population over time When in succeeding generations the amount of formal schooling for instance, is the same for the entire age range from 25 to 65 years then generalization from age differences to age changes may be made somewhat more appropriately Such equalization, however, is in the future it was not true of the past

The effect of schooling on test score, however, can be demonstrated in a cross sectional study Tuddenham's study is one such study Another comes from the Psychological Corporation s standardization of the new Wechsler Adult Intelligence Scale About 15 years ago, David Wechsler published his now well known Wechsler Bellevue Intelligence Scale, a scale comprising eleven subtests On the basis of the 1939 standardization, Wechsler interpreted the test results for different adult ages as evidence that intelligence was at its maximum at or near the twenties from which point it declines steadily At the beginning of this year, the Psychological Corporation issued a restandardized Wechsler Adult Intelligence Scale based on tests given in the 1950 s The manual for the new test shows that the total scaled score increases steadily from the teens to about age 35 years and that the subsequent decline is very much less than Wechsler projected on the basis of the 1939 standardization (15) It must be emphasized that the 1950 cross sectional samples were chosen to be representative of the population of the United States for each specific age group tested Thus even in the new standardization the younger age groups had much more schooling than did the older age groups For example 65 per cent of the 55 to 64 year-olds had 8 or less years of schooling in contrast with 27 per cent of the 16 to 17 year-olds or 22 per cent of the 18 to 19 year olds (16) Even for cross sectional samples the generalization that a sharp decrement in intelligence begins in the twenties is not true The Jones and Conrad 1920 test results reflect the conditions then prevailing Wechsler s results (which he does not interpret as I do) suggest how time bound the evidence was

With the passage of time, follow up studies have become possible Lorge, in the United States Husen in Sweden and Jarl in Denmark have each shown that intelligence test scores are related to the extent of formal education For example Lorge retested with an intelligence test as adults about 34 years of age a group of individuals who had been tested just 20 years before He demonstrated that in the 20 years in general individuals maintained their ratings in intelligence test performances but that those who had completed a greater number of years of schooling

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battery to eight adults who 18 years previously had been in a group of 40 boys diagnosed as feebleminded. Seven of the eight gained on the re-administration of the 1916 revision of the Stanford-Binet given at or near age 31 years. The average increase in the intelligence quotient was more than 15 points. All eight gained on Army Alpha with an average gain of 11 I.Q. points; all gained on the Porteus maze with an average gain of 21 points. All changes are statistically significant. While it is hazardous to generalize from eight cases, the direction seems to be for maintenance or increase in intelligence test scores.

Don C. Charles (3) retested 24 adults who as children had been classified as mentally deficient by two criteria: Binet intelligence quotients under 70 *and* the inability to perform school work satisfactorily. On the Wechsler-Bellevue used as retest, 21 subjects gained on verbal I.Q. Basically verbal, performance and full scale I.Q.'s were higher than the original Binet I.Q.'s. The adults at the time of retest ranged in age from 36 to 49 years, averaging 42 years. Part or all of the gains may be a function of the different tests used. Charles, however, attributes the gain to underestimates of intellectual status in childhood.

The major emphasis of Charles' study was upon current social status of children who had been designated feebleminded. From the evidence he concluded: "Social achievement and/or test scores suggest that about 65 per cent of the subjects who tested low originally now give evidence of being in the dull normal or average range. If ability to hold a job, to maintain a family, and not to get involved in lawbreaking is an indication of adult adjustment, then it may be inferred that even the so-called dull may keep or improve upon their childhood status." Neither Muench nor Charles suggests a decrement in intelligence over the age ranges they studied. Indeed, Charles in his summary of the literature about the adult status of children diagnosed as dull in childhood suggests a fairly bright picture for adults judged mentally deficient in childhood.

The evidence about the adult performances of the mentally dull is, as has been indicated, inadequate. Nevertheless, when coupled with the reports of Owens and of Bayley and Oden, it allows the broad generalization that adults do not decline in intellectual status when changes in intelligence are appraised by retests of the same individuals. It is reasonable to conclude that intelligence is maintained within the *same* person without significant diminution through the twenties, the thirties, and the forties. Indeed, I would venture to say that for the same individuals there would be little if any loss on the average through the fifties and the sixties. Basically, I am suggesting that the cross-sectional method gives a biased estimate curve of intellectual growth, maintenance and decline (?) because

he cross-sectional approach does not correct adequately for the differ ntial educational attainments of young and old adults

Of course intelligence tests give credits for the completion of tasks hich are an undifferentiated mixture of content process and speed ntelligence test scores in the late teens and in the sixties may be based on different kinds of tasks For example Jones and Conrad concluded that In the sixth decade of life 40 per cent of total Alpha score is derived from two tests (Test 4 and Test 8) at age 10 these tests contribute only 25 per cent. Factor analysis of intelligence test scores at different ages in dicates that the tests measure different amounts of the principal com ponent at different ages In Spearman s terms the principal component (which he calls g) is the factor that is involved in the measurements of ability of all kinds and which is throughout constant for any individual (11) As estimated g accounts for the variance of test scores in the Bellevue Wechsler about as follows at age 9 for 44 per cent at age 12 41 per cent at age 15 31 per cent at ages 25 to 29 27 per cent at ages 35 to 44 38 per cent and at ages 50 to 59 50 per cent (6) This may be evidence that in the teens much of the intelligence score comes from credits for speed at least more than is true for test scores in the middle or later years Spearman as a matter of fact on much less evidence concluded that

" g increases from birth at first rapidly then more and more slowly— *until* somewhere not later than 15–16 years (and perhaps much earlier) its growth definitely *ceases* Thereafter it normally retains this maximum level unaltered *right* up to the end of life (or at least to the onset of senility) (11)

Lorge has demonstrated that older adults were penalized by *speed* on intelligence tests that were an undifferentiated mixture of power and of speed He estimated the penalty that speed places upon intellectual per formance of adults He applied a statistical correction for the speed penalty for each year following age 20 years to the data reported by Jones and Conrad The speed factor apparently accounted for the observed de cline in Alpha scores Lorge s procedure does not prove that there is no decrement it implies however that the inference of mental decline may be a function of the weights given to speed to process and to content in intelligence tests designed for school children Much of the so-called decrement is attributable to the diminished speed of reaction or the slower work tempo of older adults Certainly when intelligence is meas ured in terms of power to perform regardless of speed ability tends to remain stable for a long time span after age 20 (5)

In summary the so-called decline in intelligence does not seem to be evident when the same individuals are retested after 10 20 or 30 years

The few follow up studies allow the hypothesis that adults in their thir*ties forties or fifties will test at least as well as they did in the late* teens or early twenties Follow up evidence points to significant gains in middle maturity The gains for the most part come from test items with very large components of verbal ability, or g or of stored knowledge The follow up studies suggest moreover, that increments in test score in middle maturity are related to the recency and extent of formal education

Cross sectional studies based on more recent testing in the 1940 s and *1950 s suggest that the so-called curve of intellectual decline was a function* of the educational status of the individuals tested The empirical decline as reported for cross sectional samples in the 1940 s and 1950 s is much less precipitous and is postponed at least a decade beyond the results for 1920 and 1930 It is reasonable to expect that if the observed results were corrected for the regression of intelligence test score upon the extent of formal education the empirical decline would be even smaller The amount and quality of formal education is but one factor Adults in middle and late maturity in our culture get many other intelligence maintaining stimulations in their expanded leisure time Adults today have the advantage of more and more transactions with one another and with *the ideas and events of the modern world Easier transportation and en*hanced communication by radio television and print may postpone or prevent intellectual decline

The pitfalls surrounding the estimation of the curve of intelligence from infancy to late maturity of course are also found in the estimation of learning ability in the years following age 20 No one so far has made a longitudinal follow up study of the amount or quality of the learning of adults It would be interesting to discover if individuals who could have learned a skill or a language or methods of solving problems at age 20 could do related but different problems at age 40 or 50 or 60 It is my belief that anybody can learn at the middle or later years the same *kinds of things he could have learned in the teens or early twenties* The difference in the amount and quality of learning will depend upon the amount of time devoted to learning it This implies of course that a decrement in speed and in sensory acuity may be a concomitant of the physiologic process of aging

Again the generalizations about learning ability in older adults are a function of the appraisal of learning performance and the kinds of cross sectional samples tested Beginning with Edward L Thorndike s book *Adult Learning* (13) the experimenters have measured learning in terms of rate the amount produced per unit time or the time required per unit amount It is to be expected that decrements in rate necessarily are related to diminished reaction time or to adapted tempo When learning

however is measured in terms of accuracy or just Can it be learned? the adult in or past the middle years can and does learn Indeed Welford has suggested that older adults frequently can compensate for deficiencies in sensory acuity and reaction time by working more cautiously, by greater effort or by deliberate slowing down In his exprimental work on skill and age therefore Welford has deliberately minimized for his experiments the potential contribution of wisdom in compensating for the physiologic changes that age inevitably brings In complex tasks involving sensori motor skills Welford found that the amount of learning depends upon the extent to which the adult can control his method and his timing He states (17) that "Where such control can be fully exercised compensation is likely to occur but where the performance is narrowly constrained in either the form or timing of the constituent reactions the compensation will be virtually impossible It can be readily seen that receptor functions insofar as they deal with events of external causation impinging upon the subject are essentially less under his control than effector processes initiated by his own central mechanisms, and therefore permit less compensation for deficiencies of ability and are likely to break down sooner Where rigid constraints are placed upon effector processes effector functions are likely to break down just as rapidly as receptor Welford therefore emphasizes both time stress and speed of integrating information in measures of learning In his experiments however although time errors and trials are increased as a function of the age of the subjects tested basically the subjects could and did learn. Of course Welford cannot be certain that his older subjects were equivalent to his younger subjects in power *intelligence* education motivation and the like Currently there is no way by which it is possible to demonstrate the equivalence of cross-sectional samples Nevertheless the generalization is reasonable that an older adult can learn at later ages what he could have learned at younger age if he is allowed to use his wisdom in reducing speed to increase accuracy or by transferring from earlier acquired skills to new skills Kay cautions however that the older adult may be at a disadvantage in learning a new skill when previous experience is inapplicable As he puts it And the adult s deficiencies here primarily arise not because any retaining *mechanism* is functioning inadequately *but* rather the reverse it is holding on too indelibly to what it already holds an l is not suff*ciently flexible* to cope with new data (9) It is in the area of transfer of training that adult learning must be studied Can stored knowledge of skill *fact* attit [illegible]

W [illegible]

le [illegible]

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The few follow-up studies allow the hypothesis that adults in their thirties, forties, or fifties will test at least as well as they did in the late teens or early twenties. Follow-up evidence points to significant gains in middle maturity. The gains, for the most part, come from test items with very large components of verbal ability or *g*, or of stored knowledge. The follow-up studies suggest, moreover, that increments in test score in middle maturity are related to the recency and extent of formal education.

Cross-sectional studies based on more recent testing in the 1940's and 1950's suggest that the so-called curve of intellectual decline was a function of the educational status of the individuals tested. The empirical decline as reported for cross-sectional samples in the 1940's and 1950's is much less precipitous and is postponed at least a decade beyond the results for 1920 and 1930. It is reasonable to expect that if the observed results were corrected for the regression of intelligence test score upon the extent of formal education, the empirical decline would be even smaller. The amount and quality of formal education is but one factor. Adults in middle and late maturity in our culture get many other intelligence-maintaining stimulations in their expanded leisure time. Adults today have the advantage of more and more transactions with one another and with the ideas and events of the modern world. Easier transportation and enhanced communication by radio, television, and print may postpone or prevent intellectual decline.

The pitfalls surrounding the estimation of the curve of intelligence from infancy to late maturity, of course, are also found in the estimation of learning ability in the years following age 20. No one so far has made a longitudinal follow-up study of the amount or quality of the learning of adults. It would be interesting to discover if individuals who could have learned a skill, or a language, or methods of solving problems at age 20 could do related but different problems at age 40 or 50 or 60. It is my belief that anybody can learn at the middle or later years the same kinds of things he could have learned in the teens or early twenties. The difference in the amount and quality of learning will depend upon the amount of time devoted to learning it. This implies, of course, that a decrement in speed and in sensory acuity may be a concomitant of the physiologic process of aging.

Again, the generalizations about learning ability in older adults are a function of the appraisal of learning performance and the kinds of cross-sectional samples tested. Beginning with Edward L. Thorndike's book *Adult Learning* (13), the experimenters have measured learning in terms of rate, the amount produced per unit time, or the time required per unit amount. It is to be expected that decrements in rate necessarily are related to diminished reaction time or to adapted tempo. When learning

…mmunity As I see it, our greatest hope for future research is to gain the interest and …tive support of both industry and labor to sponsor research in the industrial situation

Although there is some question about age changes in intellectual power, Dr Lorge …as shown that speed of performance diminishes with increasing age Working in our …boratory Dr Birren demonstrated a significant reduction in speed of performance in a …umber of tasks, such as arithmetic operations, recalling words and writing words and …umbers this is in accord with other reports in increased reaction time Mr Norris in …ur laboratory has shown an age reduction in the velocity of conduction of the nerve im…ulse This reduced speed of performance with increasing age is often ascribed to a …eneral reduction in metabolism While it is true that the basal oxygen uptake per square …neter of surface area diminishes progressively with age we have found that this total …eduction can be explained on the basis of a gradual reduction in the amount of function…ng protoplasm with age, since the basal oxygen uptake per liter of intracellular water …does not change Thus we can scarcely attribute alterations in speed to a reduction in the …ate of cellular metabolism It seems more logical, especially in the light of studies carried out by Welford and his associates to look for changes in organization and coordination as the underlying factor in changes in speed of performance

In closing I wish to point out that the psychologist can offer a more optimistic view [illegible]

[illegible] the relationship between behavior and physiologic status is not too close so there is still a wide latitude of performance and behavior possible within a given framework of physiologic or health status Even though there may be a gradual loss of functioning cells in the nervous system as age increases we know that other areas of the brain can take over many of the behavior functions As I see it, one of the most fruitful areas for future research is to explore techniques whereby the aging individual can learn to transfer functions that will enable him to compensate for his physiologic losses

DR D EWEN CAMERON (Montreal Canada) I should like to ask two questions One of them may sound rather unfair perhaps at least it concerns something that has not been discussed so far that is what is actually meant by [illegible]

[illegible] by intelligence

The second question that I would like to put to the speaker is in conjecturing about the now rather doubtful decline in performance with age has he thought about the role of anticipation

In our culture we have the anticipation that the older person will be slow We have the anticipation and he has it too, that he will be [illegible]

not try to transfer from relevant learnings These failures, however, are not serious in the age range from 20 to 50 years

Intelligence and ability to learn, while not perfectly correlated, are sufficiently related to suggest that both intellect and performances using it are maintained without significant decrement through early and middle maturity The imputed decline, to a large degree, is a consequent of thinking by analogy, constrained tests, and a limited concept of what is implied by learning ability

DISCUSSION

DR NATHAN W SHOCK (Baltimore Md) In his presentation Dr Lorge has highlighted some of the limitations of currently available methods for evaluating intelligence in adults Some of these limitations can be ascribed to our use of tests which were originally designed for the school situation Hence it is not surprising that the amount of formal education possessed by the adult subject has a profound influence on the score he makes on an intelligence test

It is also clear that all of our intelligence tests measure an undifferentiated mixture of content process and speed However the methods of factor analyses as developed by Professor Thurstone and others seem to me to offer a possible solution to this dilemma The use of factor analysis methods provides a method of bringing into a single score the identified component of a number of specific subtests We already know that during growth and development there is a change in the factor loadings for a number of the abstract components of intelligence What we do not know is how these factor loadings change over the adult life span Unfortunately the original test materials devised by Professor Thurstone to measure the primary mental abilities in school and college students cannot be applied in their present form to older adults with sensory impairments Thus we need to adapt the test instruments to make them suitable for age studies However I am confident that this approach will provide valuable information

Although I recognize the importance of social competence in adult adjustment I cannot agree with Dr Lorge s proposal to include these variables under the category of intelligence We have difficulty enough in defining intelligence —let us not further confuse our thinking with the concept of social intelligence It is my belief that we had better devise new instruments designed especially to test this aspect of adaptive behavior rather than contaminate our concepts and testing devices for intelligence

Dr Lorge has justifiably emphasized the importance of longitudinal studies of changes that occur with age in a given individual As one who has been associated with longitudinal studies I have first hand experience with the costs and difficulties of carrying out such studies However I believe they are essential Unfortunately the problems of data analysis are formidable since statisticians have not developed methods for the precise comparison of measurements made over a span of time All too often longitudinal data must be analyzed by methods developed primarily for cross sectional studies

Dr Lorge has given primary consideration to studies on subjects up to the age of 40 or 50 this is not to say that tests have not been applied to individuals at more advanced age However I suspect that Dr Lorge has refrained from comment on these studies because they have been made for the most part on individuals who were residents of mental hospitals general hospitals or homes for the aged I agree that these subjects can scarcely be compared with individuals who are still residing in the community this is a serious limitation to our knowledge and can be remedied only when investigators can have access to large numbers of middle aged and elderly people who are still living in the

i.e., statements culled from the literature about which evidence was lacking I exposed this schedule to a large group of experts in gerontology The people who believed the largest number of stereotypes about aging were those in the medical professions The people who believed the least number were college professors such as I Now this is reasonable I do not see the infirm the deteriorated aging They don t come to my office or to my classrooms But they do go to doctors and they do go to specialists The consequence is that we tend to generalize from a segment of the population to all of it I make the same mistake that you do except that mine is a more optimistic error than yours

Can we do something to offset that? Yes I think that we can be much more optimistic for more of the people who are now coming into the sixties seventies and eighties I think you ought to study not only the infirm and the indigent and the needy but also those who a e ... [illegible]

who for one reason or another need support or help of one kind or another My feeling is that the first thing doctors should do is to think of the entire range of adjustment in all the aged

The second thing is that we ought to recognize that we may be doing a disservice to people who have learned an attitude toward the meaning of work to tell them they have got to get out Certainly I doubt that many of you in this room would appreciate the generalization that you are through at 50 or at 65 We need some determinative tests to estimate how well people can perform so as to assure them that their performances are within the expected normal range of activity

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DR IRVING LORGE I am a little embarrassed as a psychologist to be put on the spot again to try the difficult task of defining intelligence I can tell you that the psychologists have spent literally thousands of printed pages arriving at a decision and for the moment I suspect that they are not yet all agreed

One of the definitions of intelligence was facetiously but correctly made by my predecessor in office Professor Edward L Thorndike He defined intelligence as that which is measured by an intelligence test While that definition is facetious it is also correct Psychologists put different items and tasks into intelligence tests

Actually the basic rationale for an intelligence test was to discriminate between children who could not and children who would not learn in other words a school oriented concept

What we would like to suggest is that intelligence is the ability to learn and to solve the tasks required by the particular environment That implies a multiple approach to intelligence not a simple one Hence on some factors there may be gains in aging and on others there may be losses I may be begging the question but I recognize that I am

The second question is what about the role of participant? In my paper to be published I make the generalization that because of the increased technologic gains in the last fifty years there may be a significant difference in the amount of participation that older people have in and with the community The use of radio and television for instance on the one hand and the increased transportation facilities and the increased availability of print—all make it possible for adults to get larger and larger stimulation from one another in the transactions of daily life

I am quite convinced that the concept of old age roles put upon us largely by the conceptualization of Shakespeare in the Seven Ages of Man may not be true at all for today In Shakespeare's day longevity was not comparable to that of the western world today In general now there is an expectation of 70 years of life at birth and much more for people who manage to survive Compare it with the approximately 29 or 30 years when Mr Shakespeare was producing his plays

You should recognize therefore that there are a number of other elements involved in the comparison of older and younger people on a cross sectional basis A person who is now reaching 65 may have entered his working career 40 years ago probably at the beginning of World War I when the work week was much longer and when fewer tools were available The result is that a large part of our population may have worked much harder and exhausted itself much more rapidly than the group of youngsters who are now coming of age and who will we hope fulfill their 50 or 60 years of promise

There is no question but that we react to the roles that are thrust upon us If it is expected that we ought to be sedentary that we ought to be quiet and that we ought to be inactive we tend to behave that way

I am convinced that Dr Cameron knows the answer to the question that people do act in accordance with the roles thrust upon them This by the way may be one of the social variations that are interesting Certainly Dr Cameron did suggest that as people become older they adopt a tempo of work I am convinced that they do more than adopt tempo There is evidence that they adopt attitudes toward work The recent findings of the Nuffield Laboratory in Cambridge England suggest that older people actually adopt special attitudes toward work The older they become the more they emphasize accuracy over speed in any particular task that they happen to do

The last question was can the effects of anxiety in aging be offset? I suspect that they can be to a large degree provided we are willing to recognize two kinds of issues First I should suggest that you for the most part as people connected with the medical profession to a large degree determine the attitude toward aging itself

A number of years ago at Arden House I gave a schedule of stereotypes about aging

CHAPTER VI

EXPERIMENTAL PROLONGATION OF THE LIFE SPAN[1]

FRANK POPE WANDA LUNSFORD and CLIVE M MCCAY

Although Roger Bacon (1214–1292) stated clearly the advantage to man in having a longer potential span of life than most of his domestic animals little use has been made of this asset in research upon aging or in the study of the diseases of old age

Some of the reasons that man has failed to make much use of animals in the study of aging are the following 1) Research in this area is frustrating because the number of variables is large and the work is slow Hence graduate students cannot often be interested in such research and the interest in this field does not spread 2) There are no research institutes for the study of aging where workers can formulate long time programs and be assured of the same degree of permanency that one finds in other fields such as agricultural experiment station work 3) Due to variability among individuals as they grow older and are subjected to the hazards of diseases and the accidents of living research upon aging requires the use of substantial numbers of animals maintained for long periods Hence such research requires space which is always at a premium in medical centers and substantial funds devoted to basic research rather than toward specific diseases 4) Effective research upon aging requires cooperative work of groups of specialists if an adequate return is made upon the long time investment in animal maintenance Since agricultural colleges usually have the better and cheaper facilities for the maintenance of animals while medical schools have the better laboratories in pathology and physiology it is important that the two cooperate However, this is difficult because the physical plants are usually widely separated and the administrative staffs seldom appreciate the advantages of such cooperation

Finally after research results are obtained with animals in fields such as nutrition the obvious paths for confirmation by harmless studies with people are almost entirely blocked to researchers The place for such tests with people is in the homes for the aged the prisons and the mental

[1] This study was supported in part by Grant No H 16[illegible]8 from the National Heart Institute of the U S Public Health Service in part by a grant from the Dental Section of the Office of Naval Research and in part by a grant from the Rockefeller Foundation

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At the same time there must be general laws that apply to many individuals and even to many species of animals.

The first of these general laws might seem to be that females outlive males This has been known for human beings for about two centuries It is evident in small animal laboratories in which rats or mice are kept for the whole of life It is not well established for other species because farm animals are seldom kept for the whole of life and no one has bothered to assemble available data upon horses or registered dogs.

Occasionally however in research upon nutrition with white rats the rule is reversed and males outlive the females After white rats are subjected to long periods of retarded growth by feeding them diets excellent in quality but inadequate in quantity there is no longer a difference between sexes Hence such treatment has given the male the same favorable status as the opposite sex in combating the terminal diseases that determine the span of life Few of us can imagine the changes in our own social structure that would result from equalizing the span of life of the sexes.

Most nutritionists would like to discover a substance, or a combination of substances that could be fed to an animal with the result that the individual would lead a long healthy life terminated by a sudden demise Attempts have been made to discover such effective mixtures of vitamins proteins inorganic constituents and antibiotics but nothing has been found to be very effective above certain modest essential basic levels There may be optimum dietary mixtures but no one has discovered them

There are a number of papers in the literature which give the impression that the life span of some experimental animal such as the white rat was lengthened by feeding it some substances such as calcium salts vitamin A or an increased allowance of milk. One needs to examine such data from at least two angles before they are applied in human nutrition In the first place one needs to determine if the tests upon the animals such as the rats were valid Long time studies with animals are subject to numerous pitfalls and statistical validity does not ensure that the results can be repeated Repetition is essential In the second place one must always ask if the studies with test animals were sufficiently similar to conditions found in man that application is justified

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First we know that animals such as the white rat grow old and die within a period of two years with many of the terminal d
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hospitals There are hundreds of institutions in which active research programs should be in progress dealing with the long time use of specific *foods* such as butter or eggs or sugar or hydrogenated fats or salt but almost nothing is being done Such studies would bring new interests into the lives of thousands of people because they would appreciate that they were sharing in attempts to develop ways of better nutrition

We will continue to make almost no progress in such institutions until 1) we can finance such studies and induce young people to undertake them as their life work and 2) we can relieve institution administrators of enough of their burdens of management so that they can have time to familiarize themselves with methods of research and assume the important administrative roles that are required to make human studies progress

It is evident that we have the knowledge and techniques in the physical sciences for making great advances in regard to aging but we lack these assets in social outlook and in institutional administration

Europe is more backward than America in facilities for long time animal research but the Scandinavian countries have done better than we in making use of their institutions in research upon tooth decay and calcium metabolism in old age At the time of the Physiological Congress in Russia twenty years ago there were already paper plans for research institutes upon aging but if any fruit has come from these it remains little known

In animal research there has long been some belief that a form of suspended animation might prolong the span of life In the old physiology texts such as that of H Milne Edwards published in 1881 one finds attention given to the dehydration of rotifers as a means of preventing the completion and termination of a life cycle The botanists have long concerned themselves with the length of time that life could be preserved in a dormant seed

This in turn introduces the possible interrelationships between such phenomena as hibernation the length of life and diseases of old age The *possibility that hibernating* animals may have unique potentials in regard to life span has come to our attention recently In the course of retarding the growth of hamsters by feeding them a low intake of a very high quality diet Miss Gladys Sperling has observed that the hamsters seem less adversely affected by such retardation than are white rats Hamsters tend to hibernate during cold weather and rats do not It is possible that a hibernating animal approaches a grain of wheat in the suspension of animation as a means of lengthening the span of life

As one tries to analyze the problem of optimum performance of an animal body throughout life he readily appreciates that there are ideal combinations of such variables as dietary factors or ways of living that must vary for each individual animal in relation to the body it has inherited

At the same time there must be general laws that apply to many individuals and even to many species of animals.

The first of these general laws might seem to be that females outlive males. This has been known for human beings for about two centuries. It is evident in small animal laboratories in which rats or mice are kept for the whole of life. It is not well established for other species because farm animals are seldom kept for the whole of life and no one has bothered to assemble available data upon horses or registered dogs.

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If we examine the sta[illegible]
mental animals in the st[illegible]
facts emerge

First, we know that animals such as the white rat grow old and die within a period of two years with many of the terminal diseases of man. Thus after two years old rats have fragile bones decayed teeth weakened lungs diseased kidneys and tumors but seldom do they show much evidence of cardiovascular diseases.

Next we know that we can extend the life span and modify the terminal diseases of old age in the white rat by retardation of growth This result is certain and has interest because it teaches us we need not face frustration in the field of animal research in longevity

In the choice of research animals one needs to consider their specific diseases Of species available today the dog seems the nearest to man The rat has many assets but its chief liability is bronchiectasis There is some hope that this disease may ultimately be brought under control and hence improve the usefulness of rats for old age research The recent progress of Sims and Berg gives hope of prevention or control of this disease in rats Today every long time study of rats whether it concerns reproduction pharmacology, toxicology, psychology or endocrinology, is faced with results subject to profound modification in the latter half of life because of the high incidence of pulmonary disease

In contrast to the white rat the dog seems to have lungs that function quite well in old age The lungs of hamsters also seem more resistant to disease during old age than are those of rats Furthermore hamsters tend to live slightly longer than rats and to develop forms of arthritis that are worthy of intensive study

In experimental animals the best way to extend the life span is through partial starvation This is effective if started even in middle life However it is most effective if started with very young rats so that the growth is retarded The normal span of life for the white rat falls between 500 and 700 days but it is easy to produce substantial numbers of rats that are over a thousand days of age and a few that exceed 1100 days by keeping them underfed for much of life upon diets of very high quality Such procedures of underfeeding profoundly modify terminal diseases This was observed by Moreschi about 50 years ago when he found he could not transplant tumors into underfed mice (1) Too little attention has been given to this basic problem of why the internal environment becomes unfavorable for the development of tumors when rats or mice are fed diets rich in all essentials but inadequate for the body in terms of energy sources

Under such conditions the body probably burns part of its essentials as fuel while the minimum amount of such materials as vitamins and essential amino acids is used to keep living cells functioning Both the late C M Jackson of Minnesota and L B Mendel of Yale had some insight into these interrelationships between retarded growth and length of life in white rats However they did not design extensive experiments to test their concepts

When the life of an experimental animal is extended by means of retarded growth part of the body seems to age at a regular rate Thus the bones grow old and fragile although they increase in size after the re

tardation is ended Chronic diseases afflict the animals more slowly than normal The hair and skin retain much of the appearance of youth

When white rats are allowed to grow at normal rates but are fed diets that differ in type it is possible to have the same incidence of diseases in old age and the same mean span of life but to have very different conditions of some organs Thus if rats are fed nothing but diets of mineralized fresh milk the teeth remain free of decay until the end of life When life ends in such animals the bones are also denser than in animals fed mixed diets Thus parts of the body may change but the over all deterioration from diseases remains the same

Most of the secrets of extended life from the retardation of growth remain to be unravelled

During the past year we have made a new use of retarded growth to study aging of rats combined in parabiotic union figure VII Nearly a century ago French physiologists initiated studies of white rats united in parabiotic unions so that they shared most of the circulating fluid through capillary circulation In exploratory studies we first prepared two pairs of rats with the help of Dr B F Kamrin One of these pairs survived for a period of 597 days which is equal to about 53 years in the case of man We killed the pair at this age because one had developed what seemed to be a chronic bladder infection This indicated that such pairs could survive into relative old age



Fig VII Parabiotic union between

During the past summer the following combinations of animals were united by Dr Frank Pope (1) litter mate rats age 2 to 3 months (2) non litter mate rats of the same age (3) litter mate hamsters (4) combinations of rats of widely different ages

Seventeen pairs of the last were prepared in July and early August 16 were alive in mid October

The mean age at the time of *operation for the older* members of the pairs was 261 days while that for the junior members was 43 days On November 11 1955 the seniors of the pairs had a mean age of one year The mean difference for members of the pairs is 218 days This age difference *represents* about one third of the span of life of a normal rat or *about an* equivalent of 22 years for man

To prepare these parabiotic unions special techniques were used in preparing the animals to reduce the surgical risks to a minimum In the first place a succession of litters was produced using the same dam and sire or a closely related sire Thus one had rats of different ages from the same parents In order to have rats of the same size at the time of operation the older rats were retarded in growth and hence were equal in size to infant rats while in age they were equivalent to adults If one compares these rats to men one can say that it is equivalent to uniting a 4 year-old boy and a 26 year-old man

Some observations in making these unions were first the severe loss of hair which lasted for two to four weeks One may ask if this is a reflection of emotional disturbance In the next place some of the older rats in the combination tended to attack their younger mates and inflict severe injuries upon the head The anesthesia provided special problems because these rats of two different ages had different requirements even though the bodies had the same weights

Both sexes have been used in these parabiotic unions between animals *of different* ages but not *opposite* sexes *This needs to be* attempted in time to determine if the female in a pair can exert her favorable influence upon the span of life

One problem that has been encountered in this work is a condition which *has been much studied especially by the Germans This is* called parabiosis disease One of a pair seems to drain the nutrients from the other with the tail and ears becoming very blanched in the donor while the other has deeply pigmented tail and ears

It has long been believed that rats retarded in growth accelerated their growth rates when allowed adequate food This was anticipated as a source of difficulty in making these parabiotic unions but no evidence has been found that the pair of very different ages grow at unequal rates

Parabiotic unions between young hamsters of the same age have proven

satisfactory Since the hamster seems relatively easy to retard in growth it may prove more satisfactory than the rat for union of animals of different ages

Man has it within his power to profoundly modify the life spans of animals and the diseases that accompany their aging

DISCUSSION

DR BENJAMIN N BERG [New York, N Y] Dr McCay is a pioneer in the systematic study of nutrition in relation to the aging process and his observations on increased longevity in rats by retarding their growth provide a useful tool in studies on aging Most important is his emphasis on the integration of the two processes and the profound effects of nutritional factors upon them

Under the conditions of his experiments he has shown that retardation of growth appears to delay the development of disease and thus lengthens the life span of the rat. Particularly interesting is his observation that optimal growth is not necessarily conducive to greatest longevity, a concept which is at variance with that of many investigators who however, h [illegible]
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As Dr McCay points out few workers are engaged in experimental studies on the relation of nutrition to longevity Because of the nature of the problem, progress is slow even when using an experimental animal with a relatively short life span such as the rat In order to arrive at statistically valid conclusions for a single experiment, large numbers of rats requiring considerable laboratory space, are necessary, and a period of three to four years must elapse before results are obtained making this type of investigation very costly Meticulous attention must be given to details such as constant temperature, humidity, and lighting avoidance of crowding and gentle handling of animals These environmental conditions can profoundly influence the outcome of an experiment Also the results in one laboratory cannot be compared with the findings in anot[illegible]
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It has long been believed that rats retarded in growth accelerated their growth rates when allowed adequate food This was anticipated as a source of difficulty in making these parabiotic unions but no evidence has been found that the pair of very different ages grow at unequal rates

Parabiotic unions between young hamsters of the same age have proven

This I think should make us wonder whether the average age of death is not more a reflection of the incidence of disease than any characteristic of the animal species

In conclusion it is fortunate that the many variables which make research so difficult in the study of nutrition in relation to longevity have not deterred Dr McCay from making important contributions in this field

Dr Ralph Gerard (Ann Arbor, Mich) I would be glad to have Dr McCay tell us whether the connections between these parabiotic animals are still limited to the skin vessels or whether he has succeeded in getting a more intimate connection through livers or other internal organs and if not the later, whether he feels that the connection available through the skin is a sufficient communication to test fully all the problems in which he will be interested

I am not certain that I entirely followed the point that Dr Shock was making Of course many organisms tend to die off not because they reach a prescribed termination of the biologic processes but because of intercurrent accidents This is borne out at least in the case of the longest lived organisms the sequoias which are notoriously resistant to fungus and other infections This has been suggested as the reason for their longevity On the other hand has it not been possible to breed pure strains in a variety of organisms—Paramecia and flies and even mammals—which without evidence of a difference in susceptibility to intercurrent disturbances have widely different survival curves?

Dr Ernest M Greenberg (New York, N Y) I have a question that is closely related to a point that Dr Shock made which I would like to raise more specifically

I would like to know more about Dr McCay's studies particularly what proportion of the deaths in these colonies have been due to diseases or to demonstrated senile changes in old organisms if the bulk of the deaths are due to diseases are not the data more relevant to the courses and causes of disease than they are to the life span of organisms?

Clive McCay I should like first to try to answer the question about the parabiotic animals To date I think we are getting circulation only through skin union However, it is surprising that we could get that between the young and middle aged animals [illegible]
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Growth is optimal according to Zucker's standard and reaches a peak at about 5?0 days in males and 6?0 days in females. Later there is a plateau and then a decline in the growth curve when disease sets in.

Because of our interest in the pathologic findings, many old rats have been killed before they have completed their potential life span. Therefore no attempt has been made to determine whether individual animals attain the extreme longevity of some of Dr McCay's rats. Such observations are part of a longevity study planned according to Dr McCay's retardation method.

However, in terms of life expectancy the mean lifespan in our colony on an unrestricted food intake is of the same order as in his retarded animals. This discrepancy may be due to one or more of the following factors: 1) difference in rat strain, 2) difference in diet, 3) lowered incidence of pulmonary infection. This last is probably the most important factor in survival rate, as Dr McCay points out.

The same kinds of renal and cardiovascular degenerative diseases develop in both colonies, but the types of tumor differ.

Evaluation of a nutritional technique for increasing longevity must include its effect on growth, reproduction and maturity. Ideally these should not be impaired. However, all three of these natural processes are altered with the onset of disease, and it is difficult if not impossible to separate the effects of experimental technique from the effects of disease. The latter, though delayed in retarded rats, develop nevertheless and confuse observations on realimentation or other nutritional procedures.

The potential life span of a species can be determined only when disease is controlled or eliminated. This is illustrated by the increased longevity of the rats in our colony with controlled pulmonary infection.

Observations on our aging rats show that growth ceases with the development of disease. However, examination of the bones of the fore and hind legs reveals that epiphyseal union has not taken place even in the oldest animals, over 1200 days of age. Incomplete epiphyseal union in old rats has been described by Dawson, Evans and others, who tend to look upon the phenomenon as one which is peculiar to the adult rat. On the other hand, persistence of epiphyseal cartilages may indicate that further growth is possible if the nutritional impairment from disease is corrected. Therefore, rats which are now considered to be senescent may not yet have reached maturity and may be capable of further growth.

The greater longevity of female compared to male rats has been described by Dr McCay and has been fully confirmed by us. This difference in the life span of the sexes, which also exists in humans, provides a fruitful area of research in the problem of aging.

Of interest to neurologists is the spontaneous occurrence of a form of muscular dystrophy in aging rats kept on a good stock diet. The condition, hitherto not described, is the chief terminal cause of death in our colony. The disease affects principally the hind legs, and the histologic changes in the muscles closely resemble the findings in experimental vitamin E deficiency. Since the diet contains an amount of vitamin E which is adequate according to current bioassay standards, the question arises as to whether the need for this vitamin increases with advancing age.

Dr Nathan Shock (Baltimore, Md): I am very much interested in Dr Berg's report that in the rat colony nourished and nurtured by Dr Simms over these many years the life span has approached or is equal to that reported by Dr McCay for animals on a reduced caloric intake. This is because I have been impressed by the uniformity of the average age at death among rat colonies, whether they are maintained in England, Switzerland, the United States, India or in Scandinavia.

The 50 per cent mortality rate for most rat colonies has been at about ?4 months

adjustability and potentialities for valuable contributions and anything that deviates from it is of necessity inferior, not to say pathologic, so that the curve of adequacy of adjustment starts out at a low level at birth, rises to a peak in the young adult and begins to drop off at or about the involution and senescence. This attitude has become so firmly established in social organization that senescence has become entirely synonymous with decline disregarding any possibility of the search for and utilization of contributions that can be made by the aged person not *in spite* of the fact that he has become old but *because* of it. Our whole system of social organization and evaluation of potentialities as well as responsibilities inherent in the various stages of human life has been geared to this attitude which whatever its value and justification may have been in the past, has during the last half century because of the drastic shift in the age composition of the population become untenable and has led to the development of serious problems.

The fact that at the present time we have begun to be particularly alarmed at the growing magnitude of this problem has, in part at least, been conditioned by the rapid increase of the proportion of older people in our population. The young adult in assuming the role of the most successfully adjusted has also accepted the fact that he has to carry the burden of responsibility for those members of society who are either younger or older than he is and do not possess the particular characteristics that are peculiar to his age. As long as this age group constituted a substantial majority of the proportion of the population this status could be maintained without any serious difficulties. But with the rapid rise in life expectancy and the growing complexity of life situations two complicating factors were introduced.

On the one hand we find that the period of childhood and adolescence has been considerably extended and the younger part of our population has come to maintain its dependency upon the adult population for support over a longer period of time. The [illegible]

[illegible] are not ready to assume responsibilities of their own until some time in the twenties. [illegible]

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CHAPTER VII

THE PSYCHOPATHOLOGY OF AGING

WILLIAM MALAMUD, M.D.

In undertaking the discussion of this topic I considered it important to define the scope and implications of the concept of "aging" (as it will be used in this presentation) and its relation to psychopathology, indicating specifically whether and to what extent the process of "aging" is to be regarded as pathological in itself and as contributing to the development of maladjustment.

I propose to start out with the thesis that aging is a normal development in the life of the individual and as such may be regarded in a manner similar to that of the other life stages, namely, infancy, childhood, adolescence, early adulthood, and middle age. Each one of these has its own specific characteristics in regard to adjustment and, when compared with other stages, presents both liabilities and assets which do not exist in the others. The dependency and need for protection in infancy and childhood, the emotional crises of emancipation and consequent revolt in adolescence, the stress of accepting responsibilities, economic, social, and family obligations *in early maturity, present hurdles in adjustment which may be regarded as* akin to those which are introduced by the deficits following the involutional process and the onset of senescence. Running parallel to these are certain assets such as the flexibility and the high potentiality for learning in infancy and childhood, the vigor and richness of perspective of the adolescent, the strength and initiative of the young adult, which present assets that offset the obstacles inherent in the concomitant liabilities. The question comes up whether comparable assets may not be found also in the process of aging. The richness of experience, the tempering of the impetuosity and emotional impulsiveness of youth by a lifelong process of reality testing, the wisdom that develops on the basis of greater self-knowledge and the appreciation of reality demands has been given but *little consideration* both by society at large and those who are engaged in research in this field, and consequently a rather distorted view of the contributions that can be made by the aged has resulted.

An important factor in the development of such a biased attitude towards senescence is the fact that in our appraisal of it we have utilized arbitrary standards which are geared to the characteristics primarily of young adult individuals. Both society and the research worker have taken it for granted that the life period between 25 and 45 represents the optimum of

would have died earlier, have continued to live and have added to the older population in hospitals It is also true that with the great increase of people of 65 and over in the general population we would naturally expect a proportionate rise in the number of people developing psychoses characteristic of old age Neither one of these, however explains the marked increase in *admissions* of people over 65, which is entirely out of proportion with the increase of people of that age in the population in general At present, the indications are that this trend will continue unless we can gain more insight into the causes of these diseases and develop more successful methods of treatment and prevention

A study of this phase of the problem is therefore, of importance in two ways In the first place, this marked increase of such psychoses in itself presents a burden to the economy of the nation and, unless it is dealt with adequately this burden will continue to increase At the same time, however, it offers a good opportunity to investigate the factors which not only in psychoses but in maladjustments in general in people over 65 lead to the problems that develop

The bulk of these cases in mental hospitals consists of the various types of senile psychoses and the mental diseases associated with cerebral arteriosclerosis A small fraction of these cases is contributed by the so-called presenile psychoses (Alzheimer, Picks etc) and, finally there is the small but clinically important group of the involutional psychoses If we proceed from this category of
area of normal old p

more serious mental diseases Quite a number of cases in these latter categories cannot really be regarded as specifically restricted to this age group and as Cameron points out a large number of the psychoneuroses for instance, are not essentially different in nature from those that occur in younger people although certain social and psychologic problems which are particularly likely to be accentuated at this period of life tend to enhance the ease with which they affect the older people

Clinically and pathologically we have

with any degree of certainty about increase in incidence of diseases in this age bracket we refer primarily to the psychoses and more specifically to patients who have actually been

the possibility that with the rapid progress that is being made in the field of medicine and particularly in the control of those pathologic conditions to which the older person is especially susceptible may and probably will result in an even greater increase in percentage of this age group. The young adult, therefore, finds himself squeezed between two age groups in the population which, while they continue to rise in proportion as far as numbers are concerned, are not given the opportunity of participating in sharing the burdens of responsibility.

In the case of the older people this has led to the establishment of a vicious circle. On the one hand, the emphasis on the deficit in certain personality functions has completely overshadowed the consideration of assets introduced by late maturity and has resulted in enforced retirement, the relegation of potentially useful members of society to an existence marked by inactivity, lack of participation, isolation and feelings of insecurity and dependence. On the other hand, this form of existence has led to a sort of atrophy of disuse with a consequent accentuation of the deficits and a decrease in assets. This trend has been further enhanced by the great economic and social changes that have taken place in this country in the last few decades as a result of a shift from a rural, agricultural society to an urban, industrial society which failed to make provisions for older people. We are faced today with a paradoxical situation in which society is doing everything possible to increase the numbers of old people and at the same time not only neglecting to utilize the vast potentials of energy that they could contribute but actually creating conditions which inevitably lead to further breakdown of their physical and psychologic adjustment.

A survey of the present status of the psychopathology of aging clearly indicates the progressively increasing magnitude of the problem and at the same time brings to light some of the factors responsible for it and the steps that will have to be taken in dealing with it.

The most convincing evidence of the rapidly growing magnitude of this problem is clearly demonstrated in current reports of the increase in incidence of mental diseases in people over 65. A recent publication issued by the Council of State Governments which incidentally presents a very broad and comprehensive analysis of the factors responsible for this problem, provides us with some truly alarming statistics. In 1950, 8.1 per cent of the total population of the nation consisted of persons 65 and over, but at the same time they comprised about 25 per cent of patients in mental hospitals. From 1904 to 1950 the number of persons 65 and older in the population increased about *four* times, but the number of first admissions of patients 65 and over to mental hospitals soared approximately *nine* times. It is true, of course, that some of this increase is due to the fact that with better medical treatment a number of chronic patients who otherwise

would have died earlier have continued to live and have added to the older population in hospitals It is also true that with the great increase of people of 65 and over in the general population, we would naturally expect a proportionate rise in the number of people developing psychoses characteristic of old age Neither one of these, however, explains the marked increase in *admissions* of people over 65, which is entirely out of proportion with the increase of people of that age in the population in general At present, the indications are that this trend will continue unless we can gain more insight into the causes of these diseases and develop more successful methods of treatment and prevention

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Clinically and pathologically we have [illegible]

[illegible] with any degree of certainty about an increase in incidence of diseases in this age bracket we refer primarily to the psychoses and more specifically to patients who have actually been

admitted to hospitals for mental diseases We do not at present possess any valid figures concerning the incidence of any of the other psychopathologic conditions that may develop in this age group as compared with either the incidence of psychoses in this group or with the incidence of such personality problems in the population at large Indications are that they probably have been subject to a similar increase in incidence as the psychoses

From a clinical point of view, the senile, arteriosclerotic and presenile psychoses show fairly characteristic changes consisting primarily of defects in memory and some of the other intellectual functions emotional lability irritability suspiciousness and in a fairly large number, the development of projections We also know a good deal about the pathologic tissue changes that are found in each one of these diseases These I take it will be reported in detail by other participants in this program Since such pathologic tissue changes are found in the brains of persons who also manifest mental pathology it would be tempting to assume that the personality disturbances are entirely due to the tissue pathology It must be emphasized however that a number of studies have definitely shown that this is not the case The fact is that such tissue changes are not at all restricted to old people who are mentally sick A number of so called normal old people who have certainly shown no psychotic manifestations have been found on autopsy to show similar changes qualitatively and in many instances even quantitatively Actually one may find the paradoxic phenomenon of marked histologic changes in people showing no psychoses and moderate to mild histologic changes in people with severe psychoses This would lead us to conclude that there is no one to one relationship between tissue changes and clinical manifestations although some relationship can be assumed in view of the fact that deficits in certain psychologic functions as compared with what we expect in a normal young adult do occur in normal old people Such deficits have been reported in the functions of memory reaction time learning ability flexibility etc

Two questions arise out of this consideration In the first place if psychotic and other serious personality disturbances occurring in some old people and not in others cannot be entirely explained on the basis of the histologic changes then we must search for what other factors may be of importance in producing these maladjustments Secondly even if we assume that some of these personality changes are results of the histologic pathology then the question would come up what causes these histologic changes? Is it primarily due to inevitable physiologic involution or are there some other physical factors that produce such changes—particularly since they differ in intensity in individual cases belonging to the same age group? The investigations in the last area could very well utilize the infrequently occurring instances of presenile psychoses which by definition

develop in people younger than the usual old age group and their progress is much more rapid and intensive There are definite indications that disturbances in metabolism in the endocrine system and in enzyme function may play an important role in the development of such changes and if that is the case then obviously the question would come up as to whether some methods of preventing or treating such disturbances could be discovered

We are still faced with the question however as to what other factors may be involved in the development of psychopathologic phenomena in old people in general and in those suffering from psychoses in particular for as was stated above the histologic changes in themselves cannot be regarded as being the sole etiologic factors A series of studies of the involutional psychoses which in many respects are very closely related to the psychoses of old age affords useful leads in this direction These psychoses originally were assumed to have developed on the basis of biochemical and endocrine disturbances which of course are always found in people at the involutional period particularly in women Here too however further study has led to the conclusion that such is not the case A number of observations point in that direction In the first place the involutional psychoses in women have been found to occur not only at the time of the menopause but sometimes preceding it and even more frequently years after the menopause was established In such cases it was found that during the process of the menopause itself no psychotic phenomena were observed Secondly it is common experience now that the attempt to treat these psychoses with replacement therapy by a variety of endocrine substances has produced little or no effect on the psychosis itself although it has influenced some of the vasomotor and other physiologic disturbances incident to the menopause At the same time the personality disturbances have responded very favorably both to shock therapy and various forms of psychotherapy

A number of recent studies of personality organization and life experiences in both involutional psychoses and the psychiatric disturbances in old age but particularly in the former have provided us with good leads in our search for an answer to the above questions In the first place we find in such people a massing of certain personality traits such as over conscientiousness rigidity sensitivity etc which render transitions from one stage of life into another but particularly adjustment to the later years of life more difficult Secondly and perhaps because of this type of personality organization these persons tend to restrict their life interests to narrow sectors and invest most of their emotional energy ... settings fre...

later years Finally there was the impact of a series of catastrophic stress situations which they had to face at that period These were represented by such occurrences as the sudden loss of love objects (husband wife children the home etc) operations on or injuries to organs generally related to reproduction (pelvic or breast operations prostatectomies etc) and settings in which the patient was faced with curtailment or loss of social or *economic security*

The main etiologic factors therefore in the development of psychoses and other problems of adjustment in old people consist of the following

First physical changes in the organism as a whole but particularly in the nervous system the endocrine glands and metabolism Secondly the particular personality make up of the individual which renders him vulnerable *to certain types of life problems and may be largely constitutionally* determined Thirdly special social and psychologic stress situations which are particularly likely to develop at this time of life The first of these namely the physical changes undoubtedly play a role in reducing the ability of the individual to deal successfully with life problems that require flexibility of adjustment The causes of these changes may be a combination of a) wear and tear that is bound to occur through time b) damage due to infectious and toxic agents c) disturbances in the body chemistry A great deal more research is necessary to establish the actual importance of these factors in relation to the development of physical changes of age

The second etiologic factor—namely the specific personality structure—is undoubtedly of great importance and must be taken into consideration in any attempt to formulate plans for the prevention of psychopathologic disturbances at that age Inasmuch as the personality structure of an individual may be regarded as the resultant of the interaction between inherited traits and early environmental factors which mold these traits it follows that another area of research is represented by systematic genetic studies and studies of early development and the factors that influence it Such studies of both the physical factors and personality characteristics *will greatly broaden our knowledge and could serve as a foundation for future* programs of prevention

It is obvious however that at the present time and in our own generation we must accept the existence of these two factors as predisposing agents and that for an immediate program we must turn our attention to the third group of causes namely those social and psychologic stress situations which play such an important role in the development of these problems We have already referred to some of the situations that must be considered in this area Perhaps the most important and surely the most prevalent of these is the threatened loss of social and economic security and here we find one of the major factors that may be responsible for the recent in

crease in the incidence of adjustment difficulties at this age period It is here, too that we are presented with the most promising potentialities for dealing with the problem on a practical level The nature of this aspect of the problem and the social mechanisms underlying it have been mentioned earlier in this presentation Furthermore an adequate analysis of it, and suggestions as to the manner in which society can and should deal with these problems have been presented in a number of recent publications one of the most comprehensive of which is the report of the Council of State Governments We have to consider here the effects of compulsory retirement resulting in abrupt exclusion of the older citizen from active participation in and independent contribution to community functions the feelings of isolation loneliness and uselessness that are engendered by inactivity and separation from a lifelong investment of emotional interests the feelings of insecurity resulting from dependence upon support from the outside Research on this phase of the problem and the attempt to develop a positive program of dealing with it must reach out beyond the field of medicine and secure the cooperation of the whole community Society must be made aware not only of the seriousness of these problems but also of the role it continues to play in creating them Finally research in this area which so far has concentrate l largel on
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DISCUSSION

DR D EWEN CAMERON
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I refer to h s penetrating criticism of our assessment of the capaci es of the older individual on the basis of the abilities of the younger man Very r ghtly he claims that we pre judge the older man when we atempt to measure his abilities only on the basis of capacities possessed by the yo nger man We entirely negle

l y ical effort are human characteristics estimable enough when there were horses to ride and cattle to round up but less so in an age ran dly

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at t ac of his powers when he is about or 23 and that all else all subsequent years are an unhappy decline.

Th s of course is a finding which is in extraord nary contrast with the actualities of life where by common consent we hand our destinies to the surgeon and the statesman

the engine driver and the judge, the company director and the military leader of mature years years which we feel have added incomparably to the capacity of these people to be wise, far seeing to be most capable of that most central of all human concerns namely the solving of problems the extension of our mastery over ourselves and our world

May I now pass to Dr Malamud's three main categories of etiologic agents These are the agents which he has proposed as contributing as I would gather it both to normal old age and to pathologic aging

He refers to the physical changes in the organism as a whole involving particularly the nervous system the endocrine glands and metabolism

His second group is the particular basic personality make up of the individual which he sees as being largely constitutionally determined

I should like to direct my attention principally to his third category—namely the social and psychologic stress situations which are particularly likely to develop in the latter part of life

We are all governed greatly by implicitly held rarely formulated premises premises which are nonetheless (and perhaps for the very reason that they are implicit) extremely powerful in affecting our thinking

One of the premises with which we approach the individual is that the human organism is possessed of certain functions responsive to the demands of the environment and serving to adjust us to the environment and the environment to us We see those functions as breaking down primarily in response to internally arising factors or in response to overload from the environment

Our picture of the organism then is of a relatively fixed entity adjusting within given ranges to the demands made upon it as it passes from one environment to another

I would however like to suggest to you that we might get further if we saw ourselves not only as being sustained in our functional configuration by the forces which beat upon us but also as being greatly influenced by the absence of those forces In other words if our functional configuration may be distorted by an increase in the stresses to which we are exposed that configuration can be broken up no less certainly by a *removal* of those selfsame forces to which we have become adapted To illustrate this one might say that a fish well adjusted to living at the 2 mile level in the ocean will be destroyed if forced down into one of the great sea abysses at the 5 mile depth where the crushing weight of the water will break up its tissues It will be destroyed no less certainly if it is brought to the surface and exposed to the low pressures which are equally destructive to its functioning and its structure

This same idea I think is helpful in looking at the individual Dr Malamud has talked about the psycho sociologic isolation consequent upon the rural urban shift of our times

I would like to form a bridge between this idea and those ideas put forward by Professor D O Hebb concerning the effects of sensory isolation As many of you must know he has isolated the individual from sound and light and as far as possible from touch and has found that when those sensory pressures are removed the individual begins to show increasing disturbances in his thinking distortions of his body image and very considerable anxiety within a matter of a few hours Very few people can withstand extensive sensory deprivation for more than at the most three to five days

Some 15 years ago examining senile nocturnal delirium I discovered that these pa[illegible] recent memories so defective that their span of attention was limited to a min[illegible]

but interestingly enough they would report five [illegible]

beds where there was one and a multiplicity of dressing tables and windows where only one of each existed

In other words these old people who at least during the daylight hours could maintain a reasonable spatial image provided they could look around them and thereby refresh their rapidly fading retention showed a complete break up of their spatial image when one interfered with their vision

This illustrates the extent to which our functional integrity is maintained by continual pressure of incoming stimuli from the environment

Another example of the same thing is to be found in those patients who are seriously disturbed because their powers are failing—perhaps because they cannot write so clearly, or particularly because they cannot remember so accurately These are people who need the constant reassurance of accomplishment They get along well in life when every day brings them that assurance But once their capacities go down beyond a certain critical level anxiety appears

We have many built in protective mechanisms the nature of which we are only now beginning to understand And I am inclined to believe that this difficulty in relating tissue to breakdown to which Dr Malamud refers may actually be explained in part by interference with these mechanisms

I refer for instance to a screening mechanism which we have recently discovered as lying at the point of fusion between the air and tissue conduction of sound This mechanism protects us against the recognition of disturbing unconscious significances in what we communicate When you break down this mechanism as you do when you play back a recording the patient will suddenly begin to hear things in his communication which he had not hitherto recognized and may become quite disturbed

It can be well understood that under certain circumstances air conduction may be diminished in the aged individual and possibly again disturbance created

There undoubtedly exists still another screening apparatus which lies somewhere in the visual mechanism and which under most circumstances prevents us from seeing ourselves save in terms of a reasonably acceptable image If we evade this screen by looking at ourselves in a three way mirror at the tailor's we are familiar with the somewhat unpleasant revelation with which we are presented

Finally I would point to still another mechanism wh h

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quacy and that this compensation breaks down as soon as their responses become intensified i.e., when they develop a chronic anxiety state hostilities or a tensional state Under these circumstances quite serious disorganizations of behavior set in which fortunately however will again disappear once their intensification of response can be reduced

Is disorganization a more important step in breakdown in the aged than in the younger person? Yes because with increasing years there appear a growing number of latent defects which are covered up by substitutions For in

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the engine driver and the judge, the company director and the military leader, of mature years, years which we feel have added incomparably to the capacity of these people to be wise, far seeing, to be most capable of that most central of all human concerns, namely the solving of problems, the extension of our mastery over ourselves and our world.

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His second group is the particular basic personality make up of the individual, which he sees as being largely constitutionally determined.

I should like to direct my attention principally to his third category—namely, the social and psychologic stress situations which are particularly likely to develop in the latter part of life.

We are all governed greatly by implicitly held, rarely formulated premises, premises which are nonetheless (and perhaps for the very reason that they are implicit) extremely powerful in affecting our thinking.

One of the premises with which we approach the individual is that the human organism is possessed of certain functions, responsive to the demands of the environment and serving to adjust us to the environment and the environment to us. We see those functions as breaking down primarily in response to internally arising factors or in response to overload from the environment.

Our picture of the organism, then, is of a relatively fixed entity, adjusting within given ranges to the demands made upon it as it passes from one environment to another.

I would, however, like to suggest to you that we might get further if we saw ourselves not only as being sustained in our functional configuration by the forces which beat upon us, but also as being greatly influenced by the absence of those forces. In other words, if our functional configuration may be distorted by an increase in the stresses to which we are exposed, that *configuration can be broken up no less certainly by a removal of* those selfsame forces to which we have become adapted. To illustrate this, one might say that a fish well adjusted to living at the 2 mile level in the ocean will be destroyed if forced down into one of the great sea abysses at the 5 mile depth, where the crushing weight of the water will break up its tissues. It will be destroyed no less certainly, if it is brought to the surface and exposed to the low pressures which are equally destructive to its functioning and its structure.

This same idea, I think, is helpful in looking at the individual. Dr. Malamud has talked about the psycho-sociologic isolation consequent upon the rural-urban shift of our times.

I would like to form a bridge between this idea and those ideas put forward by Professor D. O. Hebb concerning the effects of sensory isolation. As many of you must know, he has isolated the individual from sound and light and, as far as possible, from touch, and has found that when those sensory pressures are removed, the individual begins to show increasing disturbances in his thinking, distortions of his body image and very considerable anxiety, within a matter of a few hours. Very few people can withstand extensive sensory deprivation for more than, at the most, three to five days.

Some 15 years ago, examining senile nocturnal delirium, I discovered that these patients had recent memories so defective *that their span of attention was limited to a minute or two at the most.* If, during the daylight hours, one blindfolded them and put them sitting in a chair in a room, within an hour they had become not only quite disoriented *but, interestingly enough,* they would report five chairs where there was actually one, six

DR. KARL M BOWMAN [San Francisco, Cal] The first point I should like to raise is with regard to state hospital admissions for the aging I think that those figures may be *in many cases*, highly inaccurate, because in some states there is encouragement to admit old persons into state hospitals, whereas other states—for example, my own state of California—have recently passed laws against admitting the so called "harmless simple case of senility," and thereby cut down the admission rate, and so figures with regard to this must be viewed with the greatest of caution

I was glad to see the viewpoint taken of the multiple causation here of the disorders of old age with no attempt to base it on purely one single cause I agree that it is primarily a concatenation of causes, and many of them stem back to earlier years of the individual's life

There is one point I would like to raise, and I am not quite sure whether this is the place for it, but as far as I can see, it is that is the social attitude of society towards the age at which an individual should be excluded from activities, and the variations which we find, which are so horribly contradictory In the armed forces you may retire very early and get a good job somewhere else in the universities, which supposedly represent a group of individuals with very highly developed intelligence, we see individuals commonly being retired at around 65 in some cases in spite of their protests Then, we see, as regards our government positions in the elective offices in the Congress and in other places there are no restrictions on age, the same is true of our judges I would raise a question about something being done in this regard

DR. WILLIAM MALAMUD I wish to thank the discussants for the very kind manner in which they treated me Their questions, as a mater of fact were actually statements, and I agree with most of them, *in fact* all of them

I might add a few points to what has been said already Dr. Cameron [illegible]

One of the points he made, however could I think, be dealt with somewhat differently I refer to the doubts he expressed (if I understood him correctly) in regard to importance of structural changes as contributing to personality disturbances

Neuropathologic changes occurring both in normal old people and those who develop psychoses undoubtedly play a *part in the development* of deficits in personality functions These would include particularly the senile plaques the fibrillary cell changes and the vascular lesions

What I tried to say in my presentation was that in the process of growth whether it be phylogenetic evolution or ontogenetic maturation [illegible]

[illegible] as particularly well *presented* in the opening pages of Plato's *Republic*, in which Kephalus in his dialogue with Socrates, told of his experience with Sophocles When Sophocles was asked whether he was not [illegible]

in turn leads to the disorganization of a widening range of all those functions and skills in which latent defects exist Like a forest of pine trees in a high wind the fall of any one starts the fall of the next

In conclusion I should like once again to leave with Dr Malamud three general questions on which I should like to have his views The first one is to what extent does he find it useful to see functional configuration as a result of forces? Second to what extent does he see the withdrawal of psychosociologic forces as being disruptive? And thirdly to what extent does he see impairment of some of the built in screens I have mentioned as being disturbing to the individual?

Dr John Whitehorn [Baltimore Md] Dr Malamud and Dr Cameron both have emphasized the term stress and the stresses characteristic of older life periods For clinical working purposes it has seemed to me very useful at times to try to find ways in which older people can keep up activities or engage in new activities which would put stresses on them in other words a stressful life with a feeling that something depends upon how one is functioning seems a very great asset in the health program

I make this comment in part to avoid too great a use of the term stress in talking about the disadvantageous features of elderly life and to ask if Dr Malamud would not also agree as it seemed at times in his presentation that stress can be a very good thing if it is stress towards some personal significance in life which I think is one of the great lacks in our older population

Dr Jack Weinberg [Chicago Ill] I would like to point out this fact that while we interpret deficits as anxiety producing matters may it not also be possible as I believe it to be that deficits are produced as a way of handling anxieties? The deficits that we may encounter in individuals in later life may actually be a manner in which this aging organism is attempting to master anxiety

If we look upon the ego as the adaptive mechanism that which is to perceive stimuli both internal and external integrate them effect action and function as a homeostatic control may it not be possible and I have the feeling that it is on the part of this ego to exclude stimuli at a time when the aging organism is unable to handle the enormous influx of these stimuli? This is certainly true of many sensory stimuli such as the auditory and visual ones It is only within this context that one could explain why the aging organism does not see too well but sees that which it should not see or it does not hear but hears that which it should not hear or is not supposed to hear

Thus one may presuppose that this aging organism is capable of seeing or hearing more than it does Is it not possible therefore that this is some sort of a defense that the organism sets up a defense expressed in terms of a deficit but which is really meant to *handle the anxiety arising out of the inability to handle the enormous influx of stimuli*

Dr Mabel Ross [New York N Y] There is an additional point on Dr Whitehorn's question We have fairly well accepted the idea that extreme stress can bring about physiologic change We have however largely evaluated that stress in relation to something which we all would appreciate as being a very stressful situation such as combat

I wonder if we have very much information as to stress as perceived by the older person? This may sound a little vague but the point that I am trying to make is that many older people with minor disabilities have a sense of being criticized and unaccepted by their social or family group Others with greater disabilities have a sense within themselves of a noncritical acceptance on the part of the people whom they value in their environment Do we know what relationship this type of stress has to the development of psychopathologic responses and malfunctioning?

CHAPTER VIII

DRUG EFFECTS AS MODIFIED BY AGING

LOUIS LASAGNA

It is not surprising that clinicians and pharmacologists have long been interested in possible relationships between age and drug effects The passing of time is obvious the change from infancy to old age is dramatic. It seems almost ridiculous to suggest that aging should *not* affect drug responses Yet obvious facts (such as the earth is flat) have a nasty habit of turning into anachronistic nonsense so that it behooves us to examine critically the evidence on this relationship

Before proceeding to some of the available data however it might be worthwhile to spend a few moments discussing the problem from an *a priori* standpoint As I have already said few people need to be convinced that the biologic unit which is the child differs from the biologic unit which is the adult

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continual exposure to experiences of many types—physiologic pathologic, and psychologic One would not be astonished to detect different "average" responses to drugs at different age levels It is not however apparent why we need *necessarily* expect differences and as it were *demand* that the data fit preconceived notions Nor is it obvious why—when differences *do* occur—the differences *need be in a* given direction no matter how reasonable the direction may *seem* *For example* if one postulates th

required transformation to an intermediary compound before *any effects* were produced might be *less potent* in such a person There is also no *compelling* reason to rule out in advance the possibility that the *nature of the disease process* for which the drug is to be administered or some other *factor* will be the pre potent independent variable and will override *any possible* differences however real introduced by aging

the altar of Aphrodite but with regard to emotional factors in general, that the life of the old person is less subject to such emotional storms and leaves him free to utilize other mechanisms and other possibilities in adjustment which he did not have before

This brings me to the question which Dr Whitehorn raised, as to whether stress may not actually be useful Stress can be very useful, if it is fair and takes into consideration the ability of the person to react to a particular type of stress If you place the stress of playing a game of tennis on a person of 65 or 70 he just has not got what it takes or what he could mobilize at the age of 20 or 30, to play it If you placed that kind of a stress on him, obviously, it would not be fair nor wise in most cases

On the other hand, the type of stress situation which requires experience knowledge and wisdom is much more likely to be dealt with adequately by the older person As a matter of fact, when I stated that forced retirement and the consequent lack of opportunity to participate in social activities is deleterious, I meant that it may actually be responsible for an increase of the deficits If this is the type of stress Dr Whitehorn referred to, I agree with him

DR WHITEHORN I ll leave out the tennis

DR MALAMUD All right I was very much interested in Dr Weinberg s comment I take it that what he means is whether or not the older individual may use the deficits he has and some he may develop as a defense mechanism I think so very definitely Again society very frequently forces the old person to develop such deficits in order to ease the burden of adjusting himself to the type of useless life to which he has been condemned

Finally as far as Dr Bowman s comments go in the first place all my figures came from the report of the Council of State Governors and they have taken into consideration all the States and came to these figures on the basis of a composite picture I feel justified in trusting them and their figures Maybe California differs a little but then there may be other States in the country that go to the other extreme and thus 25 per cent of admissions was given as an over all figure

Certainly I agree with him that the social attitudes or the attitudes society takes today towards this whole problem are very definitely responsible for a great many of the problems that we have

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[illegible] therefore age should modify the response to drugs the hypothesis could be *correct without defining* [illegible]

[illegible] required transformation to an intermediary compound before *any effects* were produced might be *less* potent in such a person There is also *no compelling* reason to rule out in advance the possibility that the *nature of the disease process* for which the drug is to be administered or some other factor will be the pre potent independent variable and will *override* any possible differences however real introduced by aging

Let us now *turn* to impressions obtained by *scanning the* [illegible] texts The simplest [illegible]

that it is not simple

the altar of Aphrodite but with regard to emotional factors in general that the life of the old person is less subject to such emotional storms and leaves him free to utilize other mechanisms and other possibilities in adjustment which he did not have before

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principle one textbook will describe infants and children as more tolerant to sulfanilamide than adults (14) while another will differentiate infants children and younger adults from the aged (15) One can pair side by side statements that surgery is associated with a greater risk in the aged (16) with the statement that surgery is not as great a risk as it is commonly believed to be in the aged (17) It is sometimes possible to come up with apparently contradictory statements in the same article One author (18) making a case for an increased susceptibility to adverse cerebral effects after anesthesia in the aged undermines much of his argument by presenting data which lead to the conclusion (expressed by the author) that such episodes as are described must be extremely uncommon The supposed increased sensitivity of elderly patients to hypnotics and opiates will be countered by a claim that in the case of the belladonna group of drugs such patients are less likely to have adverse reactions than other adults and especially less likely than children (19) One could go on listing other similar statements but since the common denominator in most of the reports is a lack of data to buttress the conclusions of the authors we shall not suffer greatly from their omission

Instead let us examine some actual endeavors to correlate age with drug responses in human beings Unna (1) attempted to quantify the mean effective dose of atropine required to depress salivation in children of various age groups The approach was to find out how much drug was required to produce the same effect in different subjects The data are perhaps best represented by figure VIII 1 It is obvious that there is a great increase (six fold) in absolute dose with age This increase becomes less impressive

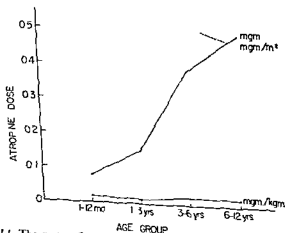


Fig VIII 1 The mean effective dose of atropine required to depress salivation of children of various age groups (After Unna (1))

ines experimental data on animals it is obvious that there is no comfort in store *for those individuals who prefer color schemes of black and white* rather than gray For example Unna (1) quotes four studies on the effects of atropine on animals one investigator found that puppies were more resistant to atropine than adult *dogs another worker came up with opposite* results in rabbits the conclusions of a third worker, who used rats tended to agree with those of the second individual nevertheless a fourth investigator, also studying rats could discern no age effects Chen (2) found alcohol and digitalis to be more toxic to mice and rabbits respectively as their age increased but in studying morphine in rats he found greatest sensitivity at both ends of the age curve with the greatest resistance being shown by rats of intermediate age Haag and Corbell (3) in contrast to the experience of Chen found digitalis just as toxic to kittens as it was to adult cats Strychnine is said to be more poisonous for young rats than for old (4) and arsenic deadlier for young silkworms than for older worms (5) Whereas rabbits show a ten fold increase in susceptibility to carbon monoxide with increasing age and rats a fifteen fold increase guinea pigs show no change whatever as they get older (6) Pentobarbital has been claimed to be less toxic in the adult rat than in the newborn rat (7) and hexobarbital supposedly less toxic to old pigs (8) The authors of the latter paper point out that of six papers which they reviewed on various barbiturates in various species only one agreed with their conclusions the others claiming greater resistance for younger animals A seventh paper found adult male animals more resistant than young male animals with reverse *findings in females* In the endocrinologic literature one finds that thyroxine is more toxic to old rats (9) whereas parathyroid extract produces greater bone changes in *young guinea pigs (10)*

In regard to reports on human beings the situation is even less satisfactory since data are harder to find Much of the clinical literature on this point is in reality in the form of *ex cathedra* opinions rather than evidence I suppose that one of the most frequent injunctions occurring in therapeutics is the one advising careful administration of drugs to people at the extreme ends of the age spectrum The implication seems to be that one need not be careful in prescribing for anyone who is not very old or very young This attitude has a certain amount of common sense appeal to it by analogy one might infer that since infants and the infirm are less able to fend for themselves in general in this world they will similarly be less resistant to the onslaughts of the overenthusiastic therapist As the literature is examined however it is again hard to come up with simple advice for the physician *One finds for example certain authors failing to* report a difference in age sensitivity to sulfa drug toxicity (11 13) while other workers claim that one exists (14 15) Even where people agree in

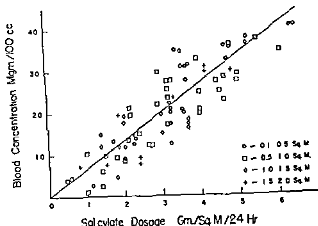


Fig VIII.3 Relation between blood concentration and salicylate dosage in patients of varying size The relation of the surface area symbols to the age of the patients is the same as that described for fig VIII.2 (After Crawford Terry and Rourke (20))

examining the data however, it was found that a straight line could be obtained relating effective dose to what was essentially the square root of body weight All differences in susceptibility previously attributed to age disappeared, although there remained a significant difference in sex response (For those of us who consider sex a more interesting and important variable than age these results seem particularly happy)

At this point it might be advisable to re-examine our problem What is the question we are asking ourselves? Are we interested in the existence of a fundamental change in reactivity to the effects of a drug as a person gets older? If this is so the problem becomes enormously complex It is relatively simple to examine the performance of patients of different age groups in response to a given quantity of drug If one does this it is ridiculously easy to show that the same absolute quantity of drug given to a baby produces results quite different from those seen in an adult given the same

weight or body area differences due to aging may become minimized or

... differential susceptibility to the effects of the drug Obtaining this sort of information is really rather difficult, although one can

(less than two fold) if one expresses dosage on the basis of body surface and essentially disappears if one uses body weight as a basis. Unna (1) also observes that variations in individual susceptibility to atropine are large in all age groups.

Crawford, Terry and Rourke (20) also accumulated data bearing on the point in question. In patients ranging from infancy to adulthood they found that in the case of both sulfadiazine and aspirin, blood concentrations were directly related to dosage of drug if the drug was given on the basis of grams per square meter of body surface. In these experiments (figures VIII 2 and VIII 3) age seems to have been of no importance whatsoever in determining the response. It is true that blood concentrations of drug are not necessarily related to therapeutic effect or toxicity, but these data at least give no support to the notion that such things as absorption, distribution, etc. of drug are radically different in the age groups represented.

Another study of considerable interest is that by Bliss, Greiner and Gold (21). In an earlier paper it had been stated that infants and young children *were found to be considerably less susceptible to the effects of digitalis than* adults. This finding was in keeping with the clinical impressions of some clinicians but at variance with the experience of certain others. On re

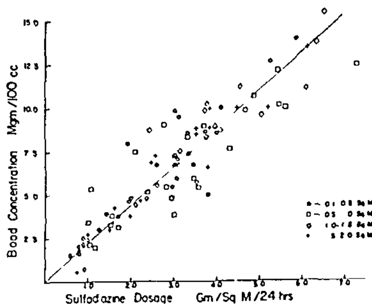


Fig. VIII-2. Relation between blood concentration and sulfadiazine dosage in patients of varying size. The symbols for surface area range in this figure comprise the following age groups: ○ (0.1–0.5 sq. m.) infants; □ (0.5–1.0 sq. m.) young children; (1.0–1.5 sq. m.) older children and adolescents; (1.5–2.0 sq. m.) adults. (After Crawford, Terry and Rourke (20).)

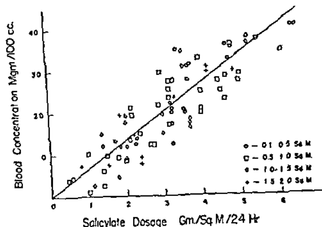


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If one shifts however, to administration of drug on the basis of body weight or body area differences due to aging may become minimized or drop out completely I suppose a basic point of comparison should be effective receptor site concentration for the drug in question If a person aged 60 requires twice as much (or half as much) drug concentration at the receptor site to get a given effect as a person aged 20

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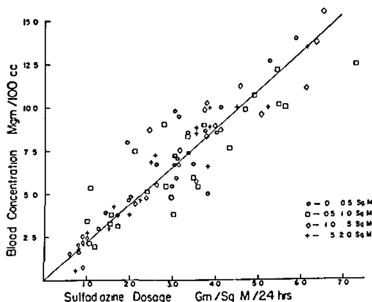


Fig VIII 2 Relation between blood concentration and sulfadiazine dosage in patients of varying size The symbols for surface area range in this figure comprise the following age groups ○ (0 1 0 5 sq m) infants □ (0 5 1 0 sq m) young children ◇ (1 0–1.5 sq m) older children and adolescents + (1 5–2 0 sq m) adults (After Crawford Terry and Rourke (20))

sponse to drugs increased with age. It is possible that the mean effective dose for a drug might not change particularly, but that the shape of the dose response curve might be relatively steep or relatively flat according to age group. Presence of a relatively flat curve would increase the difficulty of defining an "optimal dose" for an age group, since the extremes (those who do not react easily or who overreact) would cover a greater spread of dosage. Such a phenomenon might explain the development of a fallacious clinical impression that *all* aged patients showed increased (or decreased) susceptibility to the effects of a drug.

It might be worthwhile to repeat at this point that age might prove to be, in many situations, a very minor determinant of drug action. There is evidence, for example, that seasonal variations of the response of rats to a barbiturate my be greater than differences between rats of varying ages at a given time of year (23). The toxic cardiovascular effects of a drug in humans are probably more easily relatable to the state of the heart and blood vessels than to chronologic age. In some situations, as in the case of psychosis, it appears more important how long a patient has been ill rather than how old he is, in predicting response to a drug like chlorpromazine or reserpine (24).

In closing, I should like to plead that attempts to correlate age with response to drugs be considered only as an initial step in enlarging our under-

[illegible] a drug the question should then immediately be asked, "What does this correlation *mean*?" Such correlations might be of considerable importance in uncovering *information* about the distribution of a drug, its metabolism, excretion, or mode of action.

A few words on this point of "correlation investigation." It is possible, as you know, to demonstrate an inverse relationship between the number of letters in the name of a month and the ease of purchasing oysters in restaurants. Such a correlation implies nothing of cause and effect, but is of certain pragmatic usefulness in buying oysters. To someone vitally concerned with the problems of oyster supply, such information would be only a starting point in uncovering more important correlations. Dr. Withering's discontent with the knowledge that a concoction of 20 or more herbs was associated with relief of the symptoms of dropsy is a classic example of the importance of asking, "What does this correlation mean?" Medicine can provide many such examples, and it is perhaps paradoxically due to the fact that correlations in medicine frequently turn out to be meaningful and not spurious that we are often tempted to accept a correlation as a basis for action and not probe it further. For a final reminder that such a habit can lead one into untenable positions, consider

make a good approximation by studying plasma (or plasma water) concentrations of some drugs

To illustrate the difficulties one can get into by neglecting problems of distribution and metabolism let us consider the case of a drug which is localized to a tremendous degree in body fat although the organ of interest may actually be the heart or the brain On the average as people get older the percentage of body weight contributed by body fat increases Therefore the same individual weighing 150 pounds at the age of 20 and at the age of 60 and given equal amounts of the same drug at these two ages would be receiving equal doses on the basis of body weight or body area Yet the plasma concentrations of the drug achieved in the two instances would be quite different A spurious differential reactivity might thus be established Under these same circumstances it might also be possible to *miss* a real correlation with age If the person at age 60 responded identically (functionally) as the person at age 20 the knowledge *that the oral* dose had been identical at both times would suggest that the reactivity of the individual had not altered with age Yet the difference in blood (and brain) concentrations produced by changes in body composition with aging should have produced a lesser effect in the 60 year old The fact that a lesser effect was not achieved would indicate that the reactivity of his central nervous system had actually *increased* over the years If the above examples based on changes in distribution of drugs seem too complex one could describe similar difficulties in interpretation of drug responses caused by differences in drug absorption at 20 and 60 years of age

What is obviously required is a good deal more work and a good deal less talk (in and out of print) On the basis of the data presented thus far it seems reasonable to expect that at least some of the commonly accepted notions about the effects of age on drug responses are incorrect For example in studies by Keats and Beecher (22) on patients with postoperative pain and in our own studies on patients with sleeping problems the incidence of untoward reactions to barbiturates in the aged has certainly been unimpressive In the latter experiments dealing with several hundred patients of all ages the only reaction to barbiturates at all reminiscent of the type so frequently described as typical of the aged was seen after the administration of secobarbital to a 17 year old boy If systematic attempts are made it should be possible to amass data which would at least allow the empiric formulation of clinically useful dicta in specific situations Even studies based on administration of a set absolute dose to patients of different ages would provide the practicing physician with rules-of thumb which should make for more effective therapeutics

The basic problem remains however of importance both theoretically and practically It would be of interest for example if the variability in re

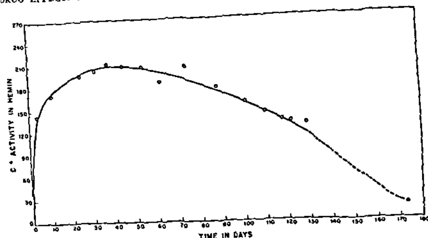


Fig VIII 4 Concentration of C^{14} labeled glycine in the hemoglobin isolated from the erythrocyte of sheep through the course of several months

With your permission, I should like to report an experiment on the question of the effect of the age of the erythrocyte on its susceptibility to hemolysis by various agents in this particular case immune hemolysis This study was carried out in association with Miss Grace Vanderhoff and Dr Otto Plescia

In this study the average life span of the sheep erythrocyte was determined by the administration of C^{14} labeled glycine to a sheep and in the first slide (figure VIII 4) we have plotted the isotope concentrations in the hemoglobin isolated from the erythrocyte through the course of several months The upward slope of the curve represents the introduction into the circulation of cells containing the labeled hemoglobin their survival and their eventual disappearance from the circulation

We can calculate from this curve the average life span of the red cell which is of the order of approximately 120 days and in this respect the sheep is like man or the dog This curve not only tells us the average life span of the sheep erythrocyte, but it also tells us that the erythrocyte is not destroyed in a random fashion but is destroyed as a function of age

In order to determine the question of the effect of the age of the erythrocyte on its susceptibility to immune hemolysis at various times during this experiment aliquots of erythrocytes were removed and were subjected to controlled hemolytic conditions so that 25 per cent of the cells would be destroyed

The cells were incubated with rabbit antisheep erythrocyte serum and with guinea pig complement and in figure VIII 5 we have plotted the susceptibility of cells at various periods in their age to such destruction If the destruction were a completely random phenomenon and the age of the cell did not have any effect on its susceptibility to immune lysis the points would actually fall all on the zero horizontal line In effect however one can observe that after an initial period of what appears to be diminished resistance to immune lysis the young adults are then considerably more *resistant to such* destruction But then as the cells begin to approach the end of their life span at the end of some three to four months, there is a marked increase in their susceptibility to immune hemolysis

I think that this study does demonstrate that when a single cell—and we are not

this statement It has been conclusively demonstrated by hundreds of experiments that the beating of tom toms will restore the sun after an eclipse (25)

SUMMARY

Although chronologic age has been shown to be correlated with response to drugs in certain circumstances, such correlation is not inevitable nor is its nature predictable At times increasing age seems to predispose to hyperreactivity, at times to hyporeactivity, and at times seems not to affect the magnitude of response in any significant way The problems involved in establishing and assessing such correlations are discussed It is suggested that the systematic collection of data bearing on this point may provide leads for important contributions to our understanding of the fate and action of drugs

DISCUSSION

DR IRVING LONDON [New York N Y] I am grateful for the privilege of participating in this meeting and for the opportunity of discussing Dr Lasagna s very thoughtful paper

Dr Lasagna has properly indicated the difficulties of drawing correlations between age and response to a drug and has pointed up the importance of considering the relations of the dosage of a drug to body weight and to physiological distribution and metabolism of the drug Concentration of the drug at the receptor site may provide a basis of comparison in evaluating responses in different age groups and yet even where the concentration of the drug at the receptor site is known the evaluation of the effect of age on the response to a drug might be difficult For example the effects of atropine which might be present in identical concentrations in the smooth muscle effector sites in individuals of different ages might be different because of differences in vagal and sympathetic tone and such differences in tone may or may not be correlated with age

The problem is therefore certainly a very complex one and facile generalizations may readily prove erroneous

In therapeutic ranges of drugs the differences may be very slight and even if significant may be difficult to define in the context of numerous other reactions which might influence a particular response In order to pursue the question of the effect of age on the response to a drug it may be useful to consider the response to lethal and sublethal doses We are repeatedly being reminded in our daily experience that the aging process does have an effect on the response to maximally stressful stimuli For example Sugar Ray Robinson who is to compete tonight in the boxing ring is only five years older now than he was at what was considered the height of his fighting career During these five years the aging process has probably taken some toll The testing of any individual response to a drug or to some other single external stimulus may not elicit a response which is demonstrably different from that which would have occurred five years ago and yet the overall response to the maximal stress of a boxing match may succeed in eliciting a series of reactions the total effect of which would represent a definite change from that which was obtained some years back

Experimental evidence for the effects of the aging process on responses to maximally stressful agents may be provided in the microcosm which the red blood cell represents

DR. IRVING LONDON [New York N Y] May I extend my remarks for just a moment, Dr Moore? I regret that there seems to be some misunderstanding and I should like to clarify one point if I may

When Dr Weiss says that the erythrocyte is a dead cell he is correct in the sense that the mature erythrocyte cannot reproduce itself Within recent years however with the focus of interest on the metabolism of the erythrocyte one cannot help but be impressed with the extraordinary metabolic activity which this cell undergoes during the course of four months after its release into the peripheral blood

The erythrocyte offers an excellent opportunity for studying the cell during various aspects of its life and can serve as a kind of model system which may permit the study of the effects of drugs and of other agents in terms of the age of a specific cell

Even while observing the caution of not attempting to extrapolate from this particular cell to the whole organism one may uncover data of fundamental biological importance which may be relevant to the whole organism

DR. LOUIS LASAGNA There is nothing more delightful for a speaker than to give a paper and have the discussers fight among themselves I feel a little like an urchin who managed to sneak into heaven on rather shaky grounds in the first place hit God with a slingshot and then instead of getting spanked sat back and watched two of the arch angels fighting

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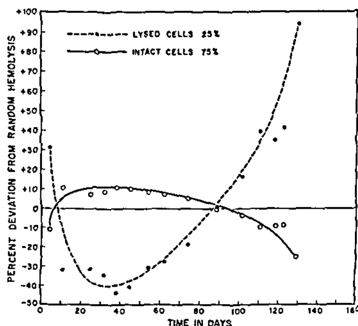


Fig. LIII 5 Susceptibility of red blood cells from sheep at various periods in their age to destruction by incubation with rabbit antisheep erythrocyte serum and with guinea pig complement

trying to extrapolate from this to a whole organism—is exposed to a *maximally stressful* stimulus such as that described the age of the cell does play an important role in terms of its susceptibility to such destruction

With the development of finer and more extensive instruments and techniques it may be possible to demonstrate differences in response to drugs administered in therapeutic dosage As Dr Lasagna has said what is needed is much more work and with this view I am in complete agreement

DR PAUL WEISS [New York N Y] I feel a bit uncomfortable about what has just been presented as an apparent incompatibility between two statements

I think that Dr London has in a way retracted his initial opposition by saying that he does not want to extrapolate the experience from a single cell to an organism for actually these are two different phenomena here and they only seem related because of the identity of the word aging that has been employed to describe both of them

The use of a single cell particularly a semi dead cell as the red cell is is a model of survival can only be compared with the decline of drug response in the whole organism after death Of course we know that even after death the heart can still respond the muscle can still respond but the brain cannot I do not quite see that the change in response of a surviving cell which is going through kinetics of decline so to speak can be at all used in answering the problem of drug response of the sum of the population which is in a stationary stage

I would like to raise this simply as an example of the caution one should observe in trying to expand from one system to another system and I am delighted that Dr London has really made that point clear in his last remark

CHAPTER IX

THE GENETICS OF AGING

FRANZ J KALLMANN

One of the notable achievements of modern medicine has been the gradual extension of the average human life span At the same time, our problems and responsibilities in this area have necessarily multiplied It is a remarkable fact that in little more than two decades, from 1930 to 1953, the equivalents of nine years—9 1 years, to be exact—were added to the total life expectancy in this country (4) This gain, accomplished chiefly by improved control over life-shortening factors, brought the general chance of survival appreciably closer to the potential length of life However, the given increase has not changed the potential life span as such, nor has it sufficiently enhanced our knowledge of the nature and extent of intrinsic longevity potentials (22)

In general terms, aging has been defined as a gradual loss of ability to maintain a constant level of physiologic equilibrium Hence, it is the ability to withstand the ensuing impairment of health that determines survival to an advanced age This capacity is known to be so variable that the many observed differences from one person to another strongly indicate the operation of gene-controlled phenomena (14, 15) That the potentiality for a long life derived from a fortunate combination of health conferring genes, can be modified by adverse life conditions in no way lessens the significance of this fundamental biologic hypothesis.

DIFFERENTIATION OF GENETIC VARIATIONS IN AGING

Genetically, a distinction is made between the effects of gene-specific processes causing premature or other pathologic disturbances in the last sector of the human life cycle and those of general genetic phenomena which produce differences in basically positive health and survival values (15) The symptoms observed in the first group of disorders are likely to be the result of one major mutant gene that follows the single factor type of inheritance

Seen in the second group of variable patterns of adjustment are gradations in normal aging potentials which result from the interaction of several or many genes and are therefore ascribable to the multifactor or polygenic mode of inheritance Extreme variations determined in this manner (through the accumulation of short life genes) are apt to produce deviations from the mean health status of an aging population, which

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tend to lead to painful experiences in interpersonal relationships, gradually overtaxing the adaptive defense mechanisms

When a psychotic break with reality occurs its symptoms are characterized by the inability to find constructive avenues for releasing anxiety generated by involutional changes Etiologically however, it is obvious that the causes of such an involutional psychosis are multiple and always include a long history of emotional instability determined genetically Admittedly the biochemical correlates of this deficiency in adjustive plasticity are still very much in need of clarification

SPECIFIC DISORDERS OF THE SENIUM

Similar uncertainties exist with respect to the genetic aspects of those pathologic conditions which are specific to the period of senescence Sufficient information is not even available regarding the least common and most easily recognizable disorders known as Pick s Alzheimer s and Jacob Creutzfeldt s diseases Here gross and relatively circumscribed brain lesions develop so dramatically and prematurely that from a genetic standpoint it would be possible to think in terms of specific disturbances produced by the effect of single mutant genes (6 10 18)

Theories of simple dominance or recessiveness have been advanced *not only* for these three special types of presenile brain atrophy but also for essential hypertension and cerebral arteriosclerosis and the total group of disorders called senile dementia However histologically verified family



Fig IX.1 Generalized presenile brain atrophy (Alzheimer)

are classifiable as pathologic Some of these deviations may be so clearly pathologic as to be indistinguishable from either a single factor type of disturbance or a so called phenocopy (a nonhereditary variation simulating the phenotype of a mutant gene)

Still another group of minus variations in adjustment to aging is due to gene controlled deficiency states physical or mental which arise before the senescent period but tend incidentally to alter the adaptive plasticity of aging persons In this category are the major psychoses specific metabolic or endocrinopathic disorders and various types of intellectual subnormalcy and emotional instability including schizoid personality traits compulsive drinking patterns and the like

PRESENESCENT TRAITS AFFECTING AGING

Exact genetic information about the manner in which presenescent maladjustment affects adaptability to aging has yet to be obtained Longitudinal studies are needed to demonstrate how specific traits tend to complicate or are complicated by the ordinary phenomena of old age Since the few studies made in this field have been related largely to chronologic rather than biologic age present appraisal of changes due to aging can be no more than a gross approximation

It would be difficult for instance to determine whether complications in the later stages of chronic pathologic conditions such as hypertension or hypothyroidism arise in the period of senescence by coincidence or as the result of a causal constitutional relationship In the case of a gene specific underproduction of the thyroid the connecting link may be a disturbance in cholesterol metabolism which affects both physical and emotional equilibrium

On the whole the impact of the senium may be expected to intensify pre existing maladjustment Old schizophrenics and mental defectives tend to deteriorate and alcoholics almost always show a marked decline in tolerance and general resistance Similarly pulmonary tuberculosis seems to have become more destructive in later life (2)

Regarding emotional maladjustment which phenomenologically falls into the involutional period the relationship between the effect of advancing biologic age and declining adaptability is demonstrated by persons distinguished by a schizoid type of behavior pattern There is substantial evidence in support of the theory that the schizoid personality structure is that of a heterozygous carrier of the schizophrenic genotype with an inadequate degree of general constitutional resistance (12) The presenescent traits most commonly associated with this type are rigidity compulsiveness and oversensitivity Along with the cumulative emotional strain arising from increasingly conspicuous signs of aging these traits

clearly substantiated in Pick's than in Alzheimer's disease The observed morbidity rates for the parents and sibs of affected persons are 19 and 6.8 per cent in Pick's disease and 10 and 3.8 per cent in Alzheimer's disease

Virtually nothing is known about the gene specific metabolic disturbances that may be at the root of these two types of early brain atrophy Conjecturally it may be stated that the given disturbances are likely to differ as much in character as do the structural changes produced by them It is regrettable that our search for verified twin cases of either type has not been successful but Dr Leon Roizin has been good enough to provide some of his material for a brief discussion of the histo pathologic differences observed between the two conditions

In Alzheimer's disease (fig IX 1) the atrophy of the brain although most pronounced in the temporal and frontal lobes is rather generalized

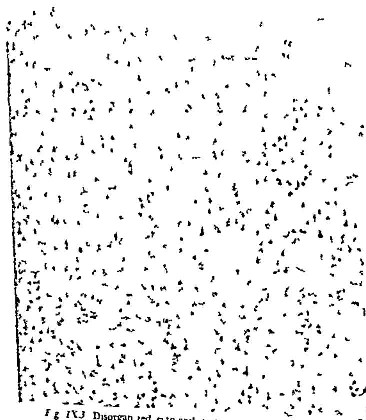


Fig IX 3 Disorganized cyto-architecture in Alzheimer's disease

data are still so scarce in this area that it would seem inadvisable to eliminate polygenic modes of inheritance, even in the fairly well studied groups of Alzheimer's and Pick's diseases According to Sjogren and his co workers (21), the theory of a simple dominant mode of inheritance has been more

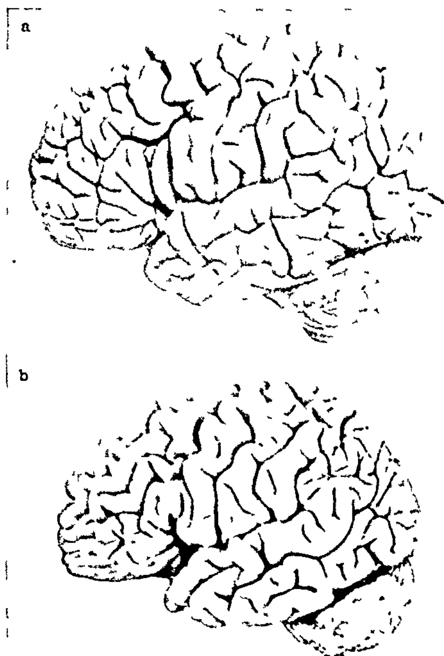


Fig IX.2 Atrophy of the brain consistent with (a) senescence (age 7?) and (b) senile dementia (age 65–73)



Fig IX.5 Circumscribed presenile brain atrophy (Pick)

the atrophy of the brain in Pick's disease (fig IX 5) is more circumscribed and usually most severe in the frontal lobes The post-central and parietal regions tend to be better preserved Microscopically the cyto architecture of the frontal lobe may show complete disorganization (fig IX 6) In this instance there are scarcely any nerve cells left and certainly fewer than in Alzheimer's disease

Using Holzer's method for glia fibers (fig IX 7) one finds a marked cortical gliosis a symptom which distinguishes Pick's from Alzheimer's disease Greatly magnified a typical cell described by Pick (fig IX 8) is characterized by an eccentric nucleus and a ballooned appearance of the cellular body

Within the cell body (fig IX 9) one sees a massive accumulation of lipid material which is highly argentophil in character This finding and the absence of both senile plaques and neurofibrillary changes are usually sufficient to differentiate Pick's from Alzheimer's disease In fact the



Fig IX 4 Senile plaques and neurofibrillary nerve cell degeneration (inset) in Alzheimer's disease

On the whole the narrowing of the gyri and the widening of the sulci are more severe than the common atrophic changes associated with the senium with or without a history of a senile psychosis (fig IX 2) Microscopically, it can be seen that the early degenerative changes in Alzheimer's disease are quite extreme (fig IX 3) The cyto architecture is so disorganized that some areas are entirely lacking in nerve cells

Application of the silver impregnation method discloses an abundance of senile plaques, and typical neurofibrillary degeneration is seen in the greatly magnified cell inserted (fig IX 4) Parenthetically it may be noted that these degenerative changes are not argentophilic

Compared with the atrophic changes observed in Alzheimer's disease,

Fig IX.7 Cortical gliosis in Pick's disease



Fig IX.8 Ballooned Pick's cell



Fig IX 6 Entirely disorganized cytoarchitecture in Pick's disease (frontal lobe)

degenerative processes in Pick's disease are so peculiar that genetically they would seem to point to a very specific metabolic disorder which has yet to be identified

Much additional genetic work is also needed in those disorders in later life in which cerebrovascular changes are the predominant feature Obviously arteriosclerotic symptoms are developed much earlier and more severely by some persons than others and equally variable is the ability to withstand cerebral damage (1) Clinically it has also been established that atherosclerosis is a disease in itself and not an ordinary concomitant of aging In fact it has been suggested by some investigators that atherosclerosis may actually be two distinct diseases the first due to defects in cholesterol metabolism or circulatory functions the second resulting from a breakdown of the structure of the elastic elements in the media of arteries accompanied by calcification The increase in deposited calcium has been shown to be associated with an increase in some amino acids which in turn may be related to the action of elastase a pancreatic hormone (9)

In any case it is particularly in the presence of a specific disturbance in lipid metabolism (known as primary hypercholesterolemia) that a fa



Fig IX.10 Dizygotic twins at the ages of 23 and 78

one-egg twins are consistently more pronounced, frequently in spite of very different environments The observed similarities extend to physical and mental signs of aging social adjustment intellectual performance, and its rate of decline The comparative histories of two *typical* twin pairs may help to illustrate this point

The twin brothers in figure IX.10 belong in the series of two-egg pairs with very similar life conditions Reared on a farm *they attended* a rural school together and then became prosperous farmers in the same district. When they were in their early thirties



Fig IX.9 Accumulation of argentophilic lipid material in Pick's disease

milial trend is found toward such pathologic conditions as coronary artery disease, essential hypertension and cerebral arteriosclerosis (7, 25). Some investigators regard dominant genotypes as the cause not only of a specific predisposition to cerebral arteriosclerosis but also of its particular localization and frequent combination with nephrosclerosis (23). However, despite the present evidence for a gene specific metabolic error being the basic cause of hypertensive disease, many of the etiologic aspects of this serious affliction of the aging are still unsolved.

Equally doubtful is the theory that the total group of senile dementias may be due to the effect of a dominant genotype of low penetrance (3, 19). Either one or two dominant genes have been assumed to be involved, one controlling longevity and one producing the pathologic changes associated with senile dementia. According to the results of our study of aging twin family units, senile psychoses seem more adequately explained by an age specific intensification of long-existing but minor deficiencies in general emotional adjustment than by a single genetic factor causing a specific type of psychopathology. This theory implies that the genetic components in the etiology of a senile psychosis consist of polygenically determined variations in age susceptible personality traits, a generally reduced level of adaptive plasticity, and those gene specific biochemical phenomena controlling growth and decline.

GENERAL HEALTH AND LONGEVITY POTENTIALS

Graded differences in general aging and longevity potentials have been demonstrated by family statistics (5, 8, 11, 20) as well as by twin studies (16, 17, 21) and are most certainly polygenic in origin. Longitudinal twin data show that compared to the limited degrees of similarity between two-egg twins or ordinary sibs, all measurable similarities between aging

TABLE IX 1

Biennial mean intra pair life span differences in same sexed twin pairs over 60

	Year of Analysis	Number of Same-Sexed Pairs		Intra Pair Life Span Differences Expressed in Months		
		All pairs	Both deceased	Male	Female	Total
Monozygotic	1948	237	32	47 6	29 4	36 9
	1950	415	68	42 9	31 2	36 7
	1952	513	76	40 7*	30 7*	35 7*
	1954	513	78	40 7*	31 6*	36 0*
Dizygotic	1948	696	36	89 1	61 3	78 3
	1950	1071	70	79 1	63 2	71 8
	1952	1226	86	79 1*	69 5*	73 7*
	1954	1226	102	69 5*	79 1*	74 6*†

* Significant at 1% level

† All opposite sexed pairs over 60 106 0 months

one is maintaining a stable home life in a suburban community where he is still active as a cemetery worker The other neither works any longer nor does he have a home of his own For 40 years he has been separated from his wife for whose sake he had changed his religion

Nevertheless both twins are in good physical health and blissfully unaware of their equally advanced state of senile deterioration In the last seven years their digit symbol scores have declined at a similar rate from 13 to 2 and from 11 to 1 Interestingly enough even the mistakes they make in substituting symbols for digits are precisely the same

In line with clinical and psychologic observations, it is shown by comparative data on the length of life of senescent twins (table IX 1) that basic variations in the human life span depend on gene specific health and longevity potentials In those pairs of our sample where both twins died after age 60 the mean intra pair life span difference continues to be much smaller in one-egg than in two-egg pairs The present total mean difference varies from 36 0 *months* in the one-egg group to 74 6 months in the two-egg group of the same sex, and to 106 0 months in dizygotic pairs of opposite sex In same sexed pairs, this difference is about the same for both sexes despite the shorter life span of the male It may also be mentioned that one-egg twin partners are more than twice as similar in causes of death as two-egg pairs of the same or opposite sex

The gene-specific basis of longevity and general health potentials in old age is confirmed by a comparison of the life spans of the sibs of senescent twin index cases with those of their parents (table IX 2) The most striking result of this analysis is the evidence for a direct relationship between parental age and the life span of the offspring The effect of

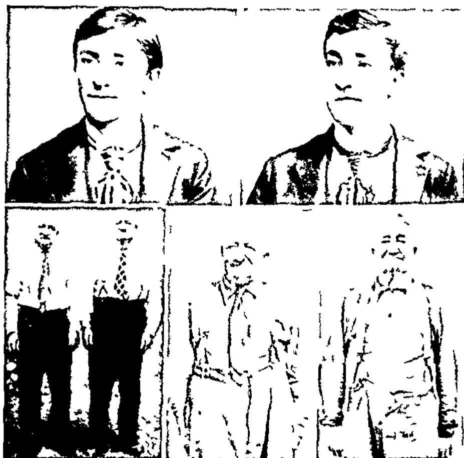


Fig IX 11 Monozygotic twins at the ages of 2[illegible], 70 and 78

each married a local girl and each had one daughter However despite the similarity of their lives they developed rather disparate personalities and patterns of aging

The younger looking twin on the left described as *prankish* excitable and somewhat extravagant complained of ill health for thirty years before retiring at age 70 The other twin who still runs his farm on his own has always been placid frugal and self sufficient He takes pride in never having seen a doctor except for an appendectomy

As to general intelligence this twin has maintained a two point advantage over his brother with vocabulary scores of 23 and 22 at the ages of 71 and 78 But in this period of seven years he has deteriorated from a score of 63 to 30 on the tapping test and from 25 to 17 on the digit symbol test [1] The corresponding decline in the twin with the slower aging patterns has been only from 78 to 67 and from 27 to 21 respectively

The one egg twins in figure IX 11 on the other hand are still remarkably alike both physically and mentally although their fortunes have differed considerably Both were employed in factories married at a young age and fathered six children each At 78

[1] The psychometric data of this longitudinal test series have been obtained by a team consisting of Dr Feingold Jarvik Mr Arthur Falek and Mr Michael Klaber The detailed results will soon be published elsewhere

pro ok ng I am no genet cist e ther by educat on or by incl nat on and I feel tl at Dr Kallmann s paper should be d scussed from two po nts of vie or rather t o aspects the theore ical and tl e pract cal

From tl e first po nt of v e I find tl at Dr Kallmann has presented a comprel ens ve and scient fically well documented statement of the scope of present day knowledge con cern ng the role played by genet cs n the process of aging H s revie of the l erature and the results of h s own mportant contribut ons lead h m to conclus ons h ch inso far as tl ey relate to the science of genet cs appear to me to be both h ghly val d an l logical and I can find noth ng w th wh ch I disagree or anyth ng that I can add to that a pect of his contr bution

If we evalua e Dr Kallmann s paper n the l ght of the present conference ho ever the question ar ses as to what bearing his find ngs have on the problems tl at are en coun ered in th s per od of l fe and to what extent genet c factors i teract v th l fe s ua ons n the development of the d sorders of old age It seems to me that e are faced l e e w th three ma n issues first the factors that determ ne the span of l fe both in the spec es as a whole and in nd duals second, the factors that determ ne the sur at potent al ty of eacl individual w th n his specific span of l fe and f nally tl e fac tors that determ ne the relati e adequacy of adjustment w tl n tl e period of survival ea h nd vidual

I th nk that we can qu te read ly agree w th D Kallmann tl at insofar as the span *of l fe is* concerned t is probably pr marily determ ned by genet c factors but I on ler wl e her we at th s conference are part cularly concerned ith that quest on unless some of s ha e tl e amb t o to d s over an elix r of l fe that could ren der us immortal or at any rate ncrease our span of l fe wh ch I take t from hat I f d in the l terature has not been creased s nce the days of C cero when he wrote h s De Senectute

We are much

chances are of rea

w tl n tl at per o

l f el l at i we v a pu o at t is t me (and in v ew of hat we heard earl er i th s conferen e about the prolongat on of the l fe of rats t sounds poss ble) to increase l e span of l fe I would sa that we would also *increase tl e* complex ty of the problem that we are concerned th today

b n

obv

s t a am speaki g now about given a certain span of l fe wl at a e our chances of survival and reach ng as near tl e ce l ng of the span of l fe as is pos l le

In some cases

a c dents infect o

u potent als tor ... as degenerat e diseases etc how these can be affected both by preven on an l treatm ent

In den ally I am glad I had the opportun ty to hear the paper for some of the material presented here was not ava lable to me at the t me when I rece ved the first y of Dr Kall a s paper I am somewhat dub ous about the importance of hered ty n Alzl e ner s d sease an l as Dr Kallmann ment oned there may be more reason to bel eve that t is hered tar ly determ ned but this *is not* certa n Some of the cases that

TABLE IX 2

Effect of parental age on mean life spans of senescent twins and their siblings

	Mother Died			Father Died			Both Parents Died		
	Below 55	55–69	70 and over	Below 55	55–69	0 and over	Below 55	55–69	0 and over
Male	55.8	58.8	59.6	56.3	57.2	60.2	51.8	61.2	61.4*
Female	64.8	64.0	66.4	63.0	64.3	65.3	62.1	61.7	66.8*
Total	58.5	59.8	62.1	58.5	60.0	61.5	55.9	59.4	6[illegible].9

* Life expectancy of the general population born in 1900 males 48.2 years females 51.1 years

parental age is independent of sex differences and expresses itself in the life spans of both sons and daughters irrespective of whether the ages reached at death by the parents are considered individually or together The comparatively highest mean age levels were attained by twin index sibships when an age of 70 years and over was reached by the mother alone or by the father alone, or by both parents There is no evidence for the operation of a sex linked factor in the inheritance of general longevity potentials

CONCLUSIONS

Based on these findings the effects of genetic factors in aging may be summarized as follows

Genetic variations in adjustment to aging may arise from gene specific traits manifested before senescence but susceptible to its overstraining effect or from specific metabolic dysfunctions peculiar to the senium or from graded differences in general health and survival values Much additional research is needed in all three categories

Since genetic phenomena are the cause of many individual differences in the degree of aging it is inadvisable to approach geriatric problems with the preconceived notion that the adjustive difficulties of the aged are more or less the same for all persons and thus conducive to management by stereotyped methods

Biologic factors advantageous to adjustment to aging include healthy and longevous parents the efficacious use of genetic potentialities for physical and mental health throughout life and the establishment of adequate emotional adjustment before senescence

DISCUSSION

DR WILLIAM MALAMUD [Boston Mass] The kind invitation to me to open the discussion of this paper was highly flattering but at the same time also somewhat anxiety

Causes of Death in a Senescent Twin Population Chapter in Analecta Genetica, Vol 4 ed by L. Gedda, Rome, Gregorio Mendel Institute, 1955 (in press)
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20 PEARL, R AND DE WITT PEARL, R. The Ancestry of The Long Lived Johns Hopkins Baltimore 1934
21 SJOGREN T SJOGREN H AND LINDGREN, A Morbus Alzheimer and Morbus Pick Acta psychiat [illegible]
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I have studied both in the literature and in our own material showed that in most of the Alzheimer cases there were no indications of hereditary influences and none of them incidentally, occurred in monozygotic twins

At the same time it would be important to consider how we can systematically prevent the occurrence of adverse life situations What to my mind is even more important from a practical point of view is the consideration of the third issue namely given a certain length of time of actual survival what are the chances of a well adjusted life and one which can be rendered more satisfactory both to the individual and to society?

These as I have pointed out in my own presentation earlier today are much more dependent upon social organization and life experiences than they are upon genetic factors and again I would like to state that when we consider the present problem that is posited by the gradually increasing number of older citizens it is here that we must look for a program that will enable people not only to survive but also within those limits, to lead a comfortable and useful life

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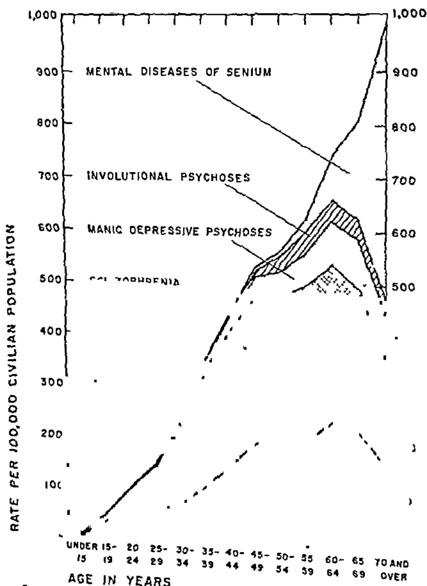


Fig X I Res dent patient rates for selected diagnoses by age state hospitals for mental disease California Louisiana Michigan Nebraska Ohio Pennsylvania Virginia 19.0

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CHAPTER X

EPIDEMIOLOGY OF MENTAL DISORDERS AND AGING

ERNEST M. GRUENBERG

THE PROBLEMS

Efforts to understand the relation between the occurrence of mental disorders and aging lead us to seek answers to certain questions: 1) What kinds of mental disorders occur more frequently among older people than among younger people? 2) What kinds of mental disorders occur most frequently among older people? 3) What is the duration of each? What is the course of each? 4) Under what conditions does each occur more frequently and under what conditions less frequently? Such information would give us a sound basis for evaluating hypotheses regarding causes derived from clinical, social and psychologic theory and for planning preventive programs.

At your Commission's request I have reviewed the literature relevant to these questions. This review has led me to three conclusions. I will state these conclusions and then briefly review the evidence on which they are based.

1. Answers to these questions can be obtained by systematic applications of established techniques for sampling populations, for locating cases and for analyzing data.

2. For data to provide answers to these questions, three assumptions must be avoided in planning and conducting investigations. First, patients who come to medical attention cannot be regarded as completely representative of those who are ill. This is obviously true where medical facilities are primitive, but it is also true where medical facilities are advanced. Second, no assumption can be made regarding the duration of any personality disorders, since this is one of the characteristics which is unknown. Third, patterns of occurrence by age of various personality disorders cannot be assumed since we wish to gain information on this question.

3. Despite the simplicity of these three statements, no studies done to date on the epidemiology of mental disorders and aging have been limited by these considerations. They have been directed at other questions and their data do not answer the questions we are asking.

patients in mental hospitals for each age The prevalence of hospitalization so to speak rises until age 60 for each diagnostic group except the diseases of the senium and the decline after that age as indicated by the tapering is mainly due to other psychoses Dr Kramer s second chart (fig X 2) shows that in the United States as a whole first admission rates to mental hospitals for all diagnostic groups falls after age 50 except for mental diseases of the senium where the rise is sharp after 60

However if we examine the first admission rates for persons over 65 by states (fig X 3) we see an enormous variation Regional chauvinists might claim that high admission rates are a sign of high civilization as reflected in the provision of hospital facilities Although such an argument would be open to question I shall not attempt to refute it as it supports my

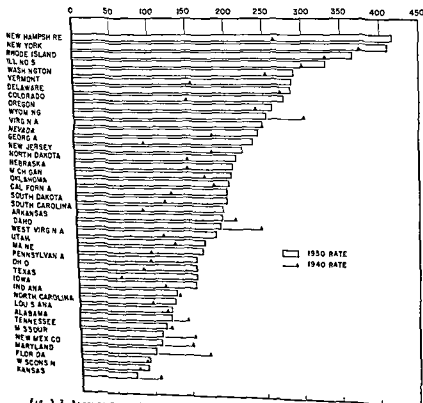


Fig X 3 Average first admission rates per 100 000 civilian population to state mental hospitals for patients 65 years of age and over selected states 1940 and 1950 Based on yearly a[illegible] for 1940 and 1941 and for 1949–19[illegible]1 Source Patients in Mental Institutions 1940 1941 1949 and 1950 and 1951 States not reporting for their entire hospital system or not reporting data by age in any of these years were excluded

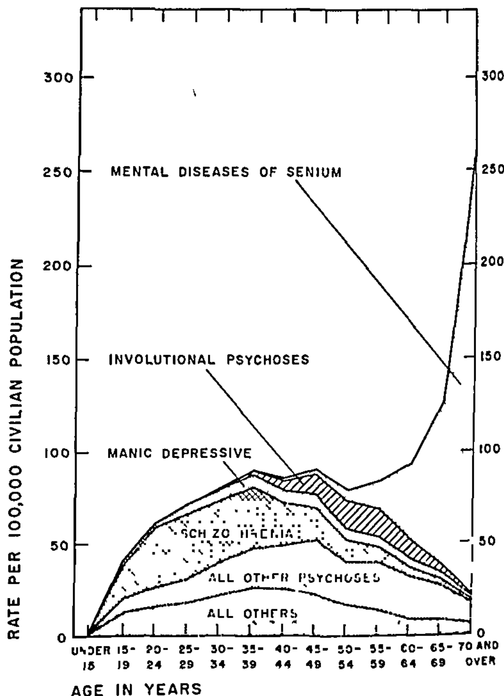


Fig X.2 First admission rates for selected diagnoses by age to state hospitals for mental disease, United States 1950

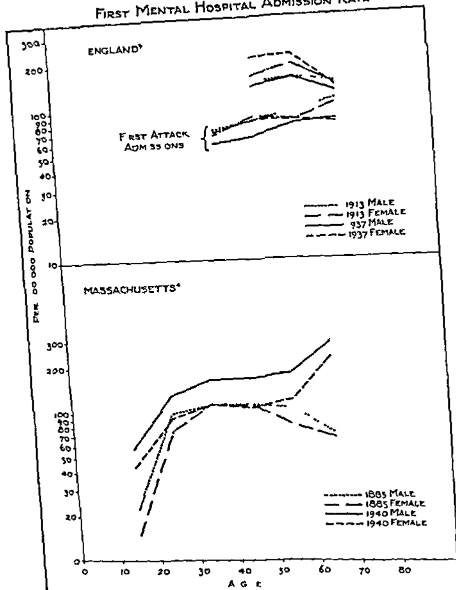


Fig X 5 First Mental Hospital Admission Rate

years when first admission rates for older people were less than for middle aged people However in recent years the first attack first admission rates in England have declined more in older people than in younger people

Such phenomena suggest strongly that mental hospital admission rates

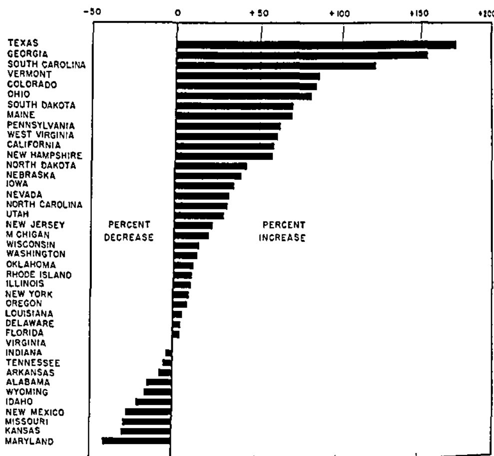
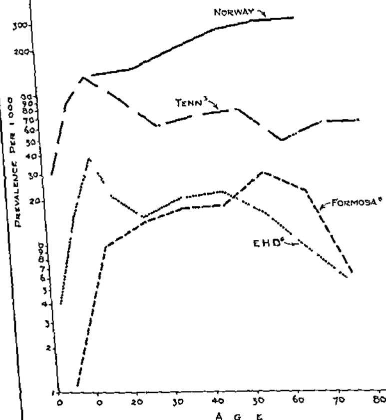


Fig X 4 Per cent change in first admission rates per 100 000 civilian population to state mental hospitals for patients 65 years of age and over selected states 1910 and 1950 Based on yearly admissions for 1910 and 1911, and for 1949–1951 Source Patients in Mental Institutions 1910 1911 1949 and 1950 and 1951 States not reporting for their entire hospital system or not reporting data by age in any of these years were excluded

thesis that mental hospitals are used differently in different times and places It may be seen that, while most states showed an increase in first admission rates for elderly persons, the amount of increase varied greatly and some states had decreases in first admission rates This is shown more clearly on figure X 4

Further evidence is available on this point Figure X 5 shows several age curves for mental hospital admissions They are not strictly comparable, but I wish to show you the difference in shape of the curves and the different ways they move as age increases To facilitate this, I have put the vertical axis on a logarithmic scale so that the slopes in the curves between any two ages represent the same proportional change in rates It is to be noted in the lower graph that aging is associated with rising first admission rates in Massachusetts in recent years in contrast to earlier



F g X.6 All mental disorders prevalence

If we now look at some of the data which are available regarding the neuroses we f n l three surveys which report neuroses by age so that age specific prevalence curves may be prepared These are shown in figure X 8 The Eastern Health District studies show an interesting bimodal curve Dr Bremer s study, based on five years of intimate experience as

reflect not only the distribution of disease but also changing patterns of use of medical facilities as well. There is other evidence that the distribution of mental disorders in a population is reflected in a peculiarly distorted way by hospital experience. Hence, to determine what kind of mental health problems occur more commonly with age, we will have to look at other sources of data in addition to hospital records.

A number of studies have been done which bring together the knowledge of all the service agencies in a community and take account of all professional sources of information about mental disorders in a population. Outstanding among these have been the pioneering Baltimore Eastern Health District studies by Lemkau, Tietze and Cooper and the Roth and Luton studies in Tennessee. Their findings for all mental disorders are shown in figure X 6. It may be seen that in Tennessee prevalence counts level off with age while the Eastern Health District counts drop sharply with age. How is it possible to account for this difference? Many possible explanations spring to mind, but there is no way I can think of to exclude the possibility that agencies in Baltimore and agencies in rural Tennessee differ in the way they relate to different age groups. Another example of studies which rely on the reports of agencies and professional persons in the community are three which searched for mental deficiency by this method. Although they differ in locale and in details of method, they share in common case findings through reports of professional agencies. Figure X 7 shows these three curves in the Eastern Health District, in a district of England (The Woods report) and in Syracuse, New York. The only one which is complete as far as age groups is concerned is the Eastern Health District study. I want to draw your attention to it particularly because it shows the sharp peak at around 14 years of age. It drops about 80 per cent in the next ten years. How can this precipitous drop in the prevalence of mental retardation in a population be accounted for? Again, many possibilities spring to mind, but one cannot exclude the possibility that our agencies are not as aware of retardation in adults as they are in children.[1] Hence, if we wish to know what effect age has on the occurrence of something like mental retardation, we cannot rely on agencies any more than we can on medical facilities to give a picture equally good for all age groups.

It is considerations such as these which lead to my first precaution: *We cannot assume that the patients who come to medical attention (or to the attention of other social agencies) are completely representative of those who are ill.*

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[1] This does not exclude the possibility that intellectual ability may rise with age as is indicated by Lorge's data; possibly this is more responsible for the decline than agency inconsistency.

ing the same phenomenon would lead us to lend some credence to this observation It should be noted that Dr Lin s study did not define a case of psychoneurosis as one which occurred for the first time during the period of observation but made use of the data available from all sources of information regardless of date of onset Hence as with mental deficiency

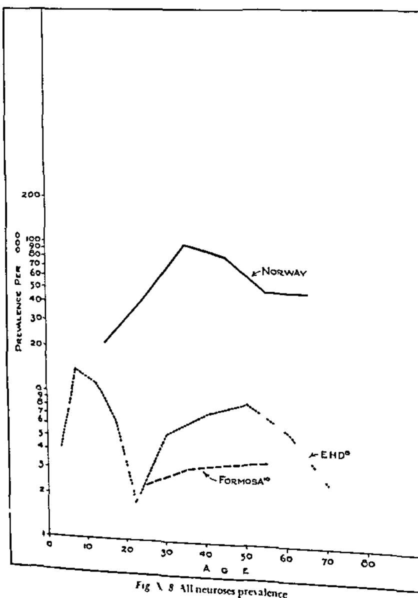


Fig X 8 All neuroses prevalence

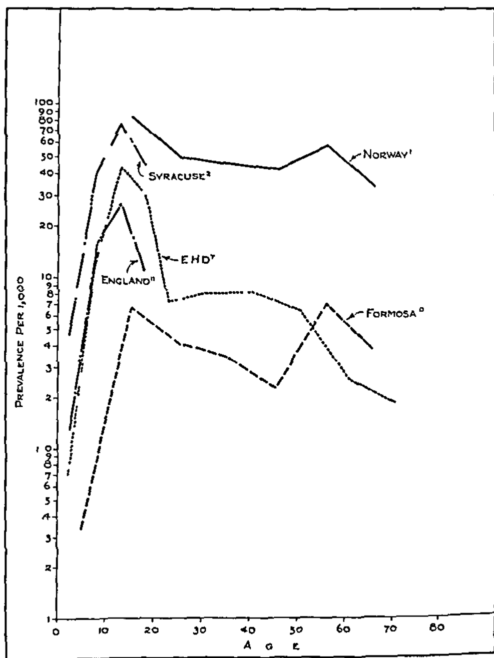


Fig X 7 Mental deficiency prevalence

the only physician in a northern Norwegian fishing village during the German occupation did not identify any children as neurotic Dr Lin's very interesting study in Formosa found a lower level of neuroses than did the other two In all three the prevalence of neuroses after 50 declined as compared to earlier years of life Three independent studies show

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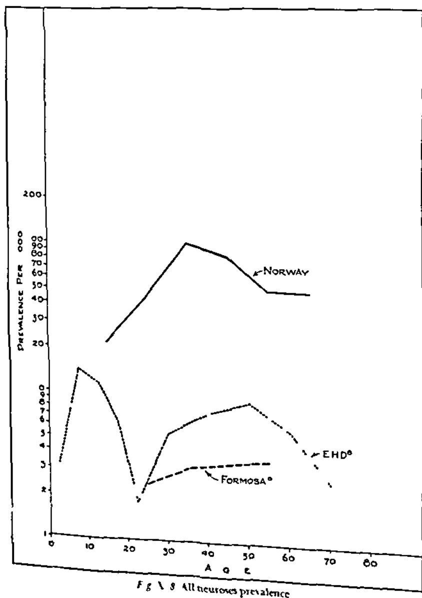


Fig 8 All neuroses prevalence

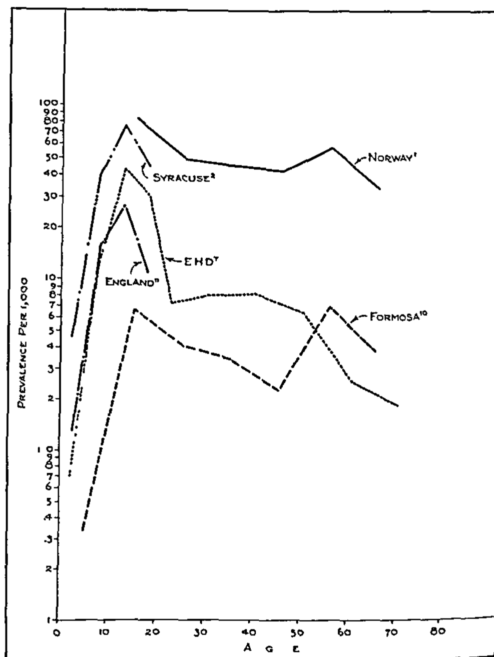


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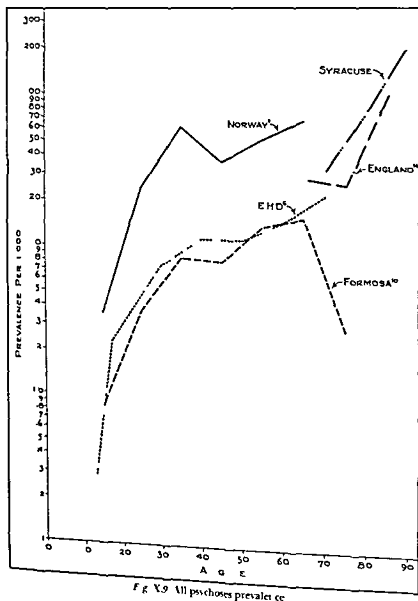


Fig. X.9 All psychoses prevalence

sclerosis or senile brain damage (12)? To answer this question it is necessary to define syndromes and case finding

one would have expected an accumulating prevalence rate with age as a person spends more and more of his life in a community and is more and more likely to come under observation. This curve in fact represents a sort of cumulative incidence regardless more or less of whether recovery had occurred or not, theoretically attenuated only by mortality and emigration. From the shape of these curves and from the shape of the previous curves on mental deficiency, it is clear that we are not justified in making any assumptions regarding duration. There is a decline with age which strongly suggests spontaneous recovery in a large proportion of cases.

Figure X 9 places five surveys in juxtaposition in a manner similar to the earlier figures. Here we are attempting to portray all psychoses by age group. The Eastern Health District shows a steadily rising line with age. The Norwegian and Formosan studies show irregularities in spite of the fact that they are attempts at cumulative incidence throughout the person's lifetime. The next to the top curve shows the results of a survey (by Sheldon in England) of elderly persons with definite mental failure. The top line shows the preliminary results of a survey in a part of Syracuse by the New York State Department of Mental Hygiene's Community Mental Health Research Unit, showing the prevalence of those who were thought to be at the time of interview as disordered as the least disordered persons in the mental hospitals.

While all of the lines on these curves represent kinds of prevalence, they represent different kinds. The English study and the Syracuse study were based on the prevalence of personality disorder present at the time of the study. The other three investigations asked whether the persons who were in the roster were psychotic persons with less precise specification of the time of prevalence. Obviously, if we assume that everyone who has a psychosis will be a psychotic person the rest of his life, and we count people as psychotic whether they have recovered or not, we cannot find out what proportion have recovered in fact. Nor will we ever learn anything definite about the duration of the illnesses we are studying. *Hence when identifying cases, assumptions regarding the duration of particular mental disorders must be avoided.*

The data on arteriosclerotic and senile psychoses present a special additional difficulty. This has to do with assumptions regarding the age of onset of these syndromes. Some investigators actually include age as a criterion in making a diagnosis. Another difficulty arises from our confusion of acute and chronic brain syndromes. The data available indicate that such states as neurosis, manic depressive psychosis and mental deficiency decline with advancing age. Is this the case or have we simply failed to recognize them in older people who may have some signs of arterio

must be evaluated more critically to see if they apply equally to people of different ages The presence of some arteriosclerotic changes must not be taken to preclude the possible existence of drug psychoses reactive de pressions or conversion hysterias If change of memory or grasp or emotional lability with age are to be studied such descriptions as normal for age must be forgotten

To avoid making assumptions regarding the duration of disorders in formation from the past must be carefully separated In such studies it is not reasonable to look more closely at the mental status of a person who is known to have been in a mental hospital thirty years ago than at the mental status of a person who is known to have run a business success fully all through his adult life More evidence of personality disorder can always be found by looking more intensely but we will never find out whether in fact those who were in hospital thirty years ago are more disturbed than those who were not unless we bar the use of such information in gathering our data

What kinds of mental disorder occur more frequently among older people? To answer this question studies are needed which observe the three precautions outlined We wish to know what disorders are more likely to have their onset in old age To find this out we would like to know the rate of occurrence of new cases per year for each age group Except for the hospital statistics none of the data cited relates to this question The surveys which have been done all ask what proportion of the popula tion at each age now has this condition this is called prevalence Preva lence figures particularly for chronic illnesses are useful in planning treatment and rehabilitation services but they are of little value in under standing which conditions favor the onset of mental illnesses and which conditions favor their prevention For that purpose we must have inci dence data The data cited indicate that the prevalence of psychoses rises markedly with age Some of the surveys indicate the prevalence of persons psychotic at the time of the survey or psychotic any time prior to the sur vey However the two most recent ones yielding similar rising curves listed only those who were mentally ill at the time of the survey

In spite of the fact that none of the studies described is satisfactory for providing answers to the questions asked each criterion is met by at least one study (Table 1) Hence it is proper to conclude that it is prac tically possible to obtain reliable information on the incidence of various mental disorders in relationship to the process of aging The basic tech niques for field study have been worked out and many of the [illegible] sures have alrea[illegible]
mation is desir[illegible]

COMMENTS

Since the population under treatment for a given disorder cannot be taken as representative of the total population with that disorder conclusions regarding the distribution of illness in the population cannot be made from such data This applies particularly to conclusions regarding the relative rates at which new cases occur in the population and to conclusions regarding the duration of illness in those who do not come to treatment Of course much of benefit can be learned by studying persons under treatment For example Redlich and Hollingshead s studies have brought out some interesting facts about patients under treatment Pollock and Malzberg have shown some important time trends and other *characteristics in patients in mental hospitals Goldhamer and Marshall* have shown that first admissions to mental hospitals with psychosis have not risen for younger people in Massachusetts during the last hundred years but that there has been a marked rise in the first admission rates for older people Meanwhile Aubrey Lewis has shown that first attack first admission rates for older people fell in England from around 1910 to the mid 1930 s All these studies are of definite value but they cannot tell us whether our elderly population actually is suffering from neuroses less frequently than people in the middle years of life

The early field studies in mental disease have left us a timeless heritage The earliest field studies were based on theories regarding the genetic origin of various mental disorders Quite properly populations were selected by family relationships to determine whether a given individual had ever manifested the disorders being studied While recognizing ages of most likely manifestation the investigation was concerned basically with whether each particular configuration of gene makeup was associated with manifestations of disorders at any age It was therefore reasonable to report the proportion of the populations which had at any time manifested the disorders under study However the viewpoint of these earlier studies seems to some extent to have become fixed Surveys asking other questions contain too little information about age of onset duration remissions and so forth By treating mental disorders as lifetime characteristics of the individual sight is lost of the fluidity of mental life of the acute short lived disorders the remitting patterns and so forth This heritage of timelessness must be given up in order to learn more about the epidemiology of mental disorders and aging If illnesses are to be defined *without reference to age* certain *criteria properly* used in clinical work must be abandoned in field research For example we cannot include progress in school work as a criterion for defining mental deficiency since school work is not expected of people of all ages Tests for intelligence

were designed to answer We forget that when we attempt to answer these questions from these data.

The merits of Dr Gruenberg's paper, I think, lie in several other areas as well The first and the most important is this the examination of the implicit assumptions and the pointing out of the implicit questions which are buried in the design of our studies in this area This is very seldom done and it particularly is very seldom done prior to embarking upon such studies

I think that he also brought to the fore perhaps by implication a series of other important areas which in actuality have been commented on by several of the speakers and discussants in the earlier part of this afternoon s session I had also thought that since some of these points had been made so excellently earlier, I would indeed tres pass on your time if I did other than merely acknowledge their importance

Our studies of epidemiology have not dealt with the question of what the conditions are which encourage a state of mental health and what the conditions are which tend to develop this disorder We have picked generally speaking the end product the specific syndrome and related that to certain other gross characteristics of the same population

We have been unable as Dr Gruenberg has pointed out to interpret the findings of *our studies* I am not now raising the question of the stability of the statistics of this particular study Regardless of the stability of those statistics our interpretations are not based upon the important issue of the context within which the disease developed and the context within which the diagnosis is made

It is possible for example that one of the differences between the findings of the *Eastern Health Study and others* has something to do with issues like this Is it possible perhaps that in these instances where lower incidences were found we would also find an attendant phenomenon the development of larger families more extended kin, and acceptance of the idea of age among the population and potentially of course also among the scientific population? The former would set the environment context for development of this disorder and the second the professional would set the context for collecting the behavior which would be treated as diagnostic clues

I would like to add to the pleas which are implicit in Dr Gruenbergs precaution two additional ones one for studies of mental health and mental disorder as they occur in their natural habitat Only in this fashion will we be able to describe the incidence as opposed to the prevalence using the distinction that Dr Gruenberg has made as well as to secure data on the conditions both personal and environmental which facilitate mental health or which if I may use the same word in this context facilitate mental disorder

It is on this point that the studies Dr Gruenberg has referred to in his paper are perhaps going to be helpful as they concern the return to the community of recovered cases from a mental hospital Followup data are important in that [illegible]
viously diagnosed persons relate to the [illegible]
ment. We may then begin to gather some [illegible]
context determines the development of symp[illegible]

I might summarize two of my own remarks [illegible]
remarks ma[illegible]
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area and [illegible]
disorder de[illegible]

With respect to [illegible]
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all wrong I merely [illegible]

TABLE X 1

Relationship of selected studies to certain weaknesses

	Confined To Service Cases	Assumes Indefinite Duration	Assumes Age of Onset	Excludes Some Ages	P = Prevalence I = Incidence
1 Lemkau *et al* (6–8)	Yes	No	No	No	P
2 Bremer (1)	No	?	?	No	P
3 Syracuse Ment Ret (2)	Yes	No	No	Yes	P
4 Syracuse Aged	No	No	No	Yes	P
5 Kramer's Hospital Admission Rates	Yes	No	No	No	I
6 Hollingshead and Redlich (5)	Yes	No	No	Yes	P
7 Eaton and Weil (3)	No	Yes	?	No	Cumulative
8 Sheldon (14)	No	No	No	Yes	P
9 Lewis (9)	Yes	No	No	Yes	I
10 Goldhamer and Marshall (4)	Yes	No	No	No	I
11 Desired study	No	No	No	No	I

is willing to pay the price for this information We must learn to ask the right questions and have the patience and fortitude to use the right techniques in seeking answers

Today we can only express opinions regarding the mechanisms by which mental disorders occur and might be prevented Tomorrow, if we do proper field studies and forego our heritage of timelessness, we may be able to give more definite answers to such questions

DISCUSSION

DR WILLIAM F HENRY (Chicago Ill) It is indeed a special privilege not merely to be able to discuss Dr Gruenberg's paper but also to discover that any bigoted or over exaggerated remarks that I choose to make may not be contradicted by my audience since I have discovered that I shall not only open but close the discussion

It is always a temptation for a psychologist to attempt to diagnose the personality of an author from his published or in this case spoken word In reading the paper of Dr Gruenberg before this presentation I came to the conclusion that Dr Gruenberg was in spite of his pleasant appearance a pessimist that he had reviewed a world of important work and concluded that one could draw no conclusions from it He drew attention to the inadequacy of medical facilities into which a great deal of time and money had gone and similarly called into question the adequacy of other social agencies into which similar amounts of extensive effort had been put

Upon more prolonged reflection however I changed my mind I think Dr Gruenberg [illegible] ly do not examine our [illegible] e are asking about the [illegible] s which Dr Gruenberg summarized at the beginning of his paper are not the questions which these studies

CHAPTER XI

STRUCTURAL ALTERATIONS WITH AGING IN THE NERVOUS SYSTEM[1]

WARREN ANDREW

INTRODUCTION

The nervous system of man while it occupies such a high position in the scale of biologic organization, seeming even to connect the physical and the psychic or spiritual, in its structural features shows fundamental similarities to other systems This system, like the others, is composed of cells and of the products of these cells Its amazing complexity is due both to the complexity of the individual cells of which it is composed and to the complicated arrangement of the many groups of these cells within the system Both the high degree of differentiation of the cells and of the pattern in which they are developed are results, according to our present concept of a process of evolution of many millions of years—from a time in the distant past when nerve cells were not so much different from other cells but perhaps slightly specialized for the reception and transmission of impulses

Although nerve cells are somewhat larger than the average cell of the human body they are still small enough to be present in tremendous numbers In the cerebral cortex of man there are estimated to be over *nine billion* individual neurons a population somewhat over four times that of the earth Investigators who have been interested in following all of the groups of cells within individual brains have had to make serial sections of these brains and even with fairly thick sections the accumulation from an individual brain runs to twenty five thousand or more large tissue sections

The high degree of specialization of the nerve cells is seen particularly in the development of their processes, which reach out, ramify, and make contact sometimes with neighboring cells and sometimes with other nerve cells or with end organs such as sensory receptors muscle, or glands even several feet away from the cell body of the neuron These processes travel so far that it is necessary for them also to be specialized, and particularly

[1] [illegible]
[illegible]
Professor [illegible]
[illegible] [illegible] ... [illegible]uation

of each age group and that these images frequently do not necessarily match up with the fact Secondly on the professional stereotype we need to examine our own viewpoints as to the assumptions underlying some of our own theoretical preoccupations Would time permit, I would like to restate these issues that were discussed earlier around the concept of stress They are extremely relevant to this problem When it comes to the use of the concept of stress particularly as it applies to the meaning of stress in interpersonal relationships we at best have no information and at worst we are handicapped by a tendency not to notice the signs that are around us and hence tend to see that which we think we ought to see

In brief summary may I merely say that in pointing out the implicit assumptions behind epidemiological studies Dr Gruenberg has done an immense service

Dr Ernest Gruenberg Since the remarks have mostly underlined some of my points I thank Dr Henry for them and thank you for the opportunity of presenting this paper

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[1] Investigation supported by a [illegible] thor's visit to the Institut fur H[illegible]
Professor Oskar Voght was supp[illegible]
ton Mass., and in part by the J[illegible] Foundation

in the matter of receiving differentiated coverings such as the sheath of Schwann and the myelin sheath The processes also have many ways of terminating They may end freely or they may end in complex bundles or in special relations with the organs which they are to innervate Here however, we shall be somewhat more concerned with the body of the cell itself This body also is a highly specialized structure While all of the features of a typical cell can be recognized in the body of the neuron the cytoplasm appears to be particularly crowded with formed elements and some of these are seen to be of a type not found in any other cells This fact has been known for many years through studies with the light micro scope and in recent times has been verified by further work using the ex tremely high magnifications possible with the electron microscope (40)

It is not uncommon to say that aging and eventual natural death are the result in higher organisms of the high degree of specialization which the various parts of these organisms have to undergo When we regard the nerve cell however we find that we are looking at the most highly special ized of cells yet that we are looking also at a type of cell which enjoys the longest life of any cell in the human body For whether or not the old adage is true that a man is as old as his arteries it surely is in general true that the nerve cells of a man are as old as he is Multiplication by mitotic division ceases to occur among the nerve cells some time late in embryonic life and thereafter the cell population remains constant except for the possible loss of such cells

The nerve cells are placed in the category of fixed postmitotics cells which have undergone their last division and which are fixed in their condition of inability to divide for the remainder of their lives (21)

Why is it that such highly specialized cells should be far longer lived than many of the less specialized cells? While we cannot point to the specific organization within the nerve cell which makes such long life possible we surely can see the need of continued existence of such cells throughout the life of an animal for they are the cells which retain the individuality of the organism and which receive and conserve the patterns of behavior in the developing animal or human being It is along the pathway of the nerve cell processes then that the impulses flow which repeated over and over again and in complicated manners eventually make us what we are Were these cells to undergo the great turnover which occurs in cells such as those for instance of the epidermis we surely could not retain the individuality of mind and spirit in the control of our material bodies

Do nerve cells die a natural death or do they continue to exist as long as the organism of which they are a part? For over half a century studies have been made which indicate that there are changes in these cells which tend to lead toward a decrease in their functional ability and eventually toward

the death and disappearance of many of them *before* the death of the organism In other words just as in an area which for some reason is be coming slowly depopulated the community may remain for a long period as such and with its own identity while people leave or drop out one by one from the census of its inhabitants so nerve cells may be removed from the cellular census of the body

The study of the death of nerve cells in the aging nervous system and their decrease in number from a quantitative standpoint is not at all an easy one Indeed there have been conflicting results in relation to the num bers of nerve cells present at various stages in several parts of the nervous system Nevertheless the mass of evidence at the present time does show that this loss not only is present but apparently is considerable in many regions In certain groups of cells as in the Purkinje cells of the cerebellum it is seen readily (fig XI 1)

Some of the difficulties encountered in such quantitative studies are due to the problems of counting nerve cells from section to section and others are due to the great variation from individual to individual which neces sarily exists in a biologic phenomenon such as the aging process Naturally, it is impossible to compare the nervous system of any one individual at differen [illegible]

va [illegible]

of [illegible] at different ages He finds a patchy appear ance due to areas deficient in cells in the *older cortex* These areas were scattered throughout the regions studied and were particularly evident in

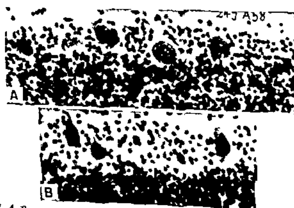


Fig XI 1 [illegible]
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in the matter of receiving differentiated coverings such as the sheath of Schwann and the myelin sheath The processes also have many ways of terminating They may end freely or they may end in complex bundles or in special relations with the organs which they are to innervate Here however we shall be somewhat more concerned with the body of the cell itself This body also is a highly specialized structure While all of the features of a typical cell can be recognized in the body of the neuron the cytoplasm appears to be particularly crowded with formed elements and some of these are seen to be of a type not found in any other cells This fact has been known for many years through studies with the light microscope and in recent times has been verified by further work using the extremely high magnifications possible with the electron microscope (40)

It is not uncommon to say that aging and eventual natural death are the result in higher organisms of the high degree of specialization which the various parts of these organisms have to undergo When we regard the nerve cell however

ized of cells yet that

longest life of any cell in the human body For whether or not the old adage is true that a man is as old as his arteries it surely is in general true that the nerve cells of a man are as old as he is Multiplication by mitotic division ceases to occur among the nerve cells some time late in embryonic life and thereafter the cell population remains constant except for the possible loss of such cells

The nerve cells are placed in the category of fixed postmitotics cells which have undergone their last division and which are fixed in their condition of inability to divide for the remainder of their lives (21)

Why is it that such highly specialized cells should be far longer lived than many of the less specialized cells? While we cannot point to the specific organization within the nerve cell which makes such long life possible we surely can see the need of continued existence of such cells throughout the life of an animal for they are the cells which retain the individuality of the organism and which receive and conserve the patterns of behavior in the developing animal or human being It is along the pathway of the nerve cell processes then that the impulses flow which repeated over and over again and in complicated manners eventually make us what we are Were these cells to undergo the great turnover which occurs in cells such as those for instance of the epidermis we surely could not retain the individuality of mind and spirit in the control of our material bodies

Do nerve cells die a natural death or do they continue to exist as long as the organism of which they are a part? For over half a century studies have been made which indicate that there are changes in these cells which tend to lead toward a decrease in their functional ability and eventually toward



Fig XI 2 Gross section of a brain of a subject with senile dementia showing atrophy of the cerebral cortex with corresponding expansion of the lateral ventricles Lesser degrees of cerebral atrophy are common in the normal senile brain

DEGENERATIVE CHANGES IN THE NERVE CELLS—A GENERAL SURVEY

We here shall speak at first only of the changes which appear to be or which very obviously are degenerative in nature for there are changes of quite another type which we shall discuss later There appear to be few if any parts of the nervous system of man which if studied carefully do not reveal degenerative changes in the nerve cells with age Studies beginning with an early investigation by Hodge (30) and followed by a large number of other workers have shown such degeneration of nerve cells both in man and in lower animals Muhlmann (38) described the age changes of ganglion cells of senile guinea pigs Dolley (25) described changes in the Purkinje cells of senile dogs Harms (28) studied the cerebr—

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the superior temporal gyrus. Actual counts show a considerable decrease in number of cells—as high in some areas as one third or more of the original number. The cells in general are spaced more widely in senile than in young adult brains. The picture, then, in many areas of the cortex is such that low power microscopic examination permits a differentiation of sections from senile and young persons, the preparation and staining of both having been as similar as possible.

The observation, however, of the *changes* which lead toward the loss of nerve cells is not as difficult. Cells undergoing these changes are present in all older individuals and indeed can be seen to arise in some cases at a fairly early age. Again, if we use the comparison of a community, we may think of one in which there is no longer any production of new individuals. In such a community viewed from time to time there will be an increasingly larger number of old individuals and individuals showing the infirmities of age. Gradually various members of the community will begin to drop out. In the same way with nerve cells, we see an increasing number of cells undergoing the changes of age and an increasing number which are reaching the stage of final degeneration.

Up to now we have been speaking in very general terms concerning these age changes. It is the problem in the present paper to discuss in detail the nature of the structural changes with age in the nervous system.

GROSS CHANGES

Gross changes which have been described include a certain amount of loss of weight of the brain. How much of this loss of weight is due to a loss of the functional elements of the brain and how much to loss of water is not known. Also, it is not known how much of the reduction in weight may be due to actual degenerative change and how much to a physiologic process.

Other changes which may in some cases be quite striking are *visible* atrophy, particularly of the cerebrum, which may lead to a widening and a deepening of the sulci and a corresponding reduction in the size of the gyri. The color of the gray matter is said to be deeper in many older brains than in young ones.

On the gross side, also, the meninges, particularly the leptomeninges, may be seen to be thickened, sometimes adherent to the brain and to one another and difficult to pick up from the cortex. An hypertrophy of the Pacchionian granulations may also occur with old age. Patches of calcification are frequently seen in the meninges of older brains. These latter may be either senile phenomena or pathologic ones.

Atrophic changes in the cerebrum, particularly in senile dementia, frequently lead to an increase in the size of the lateral ventricles (fig. XI 2).

cell of the cerebellum with its pear shaped body, shrinkage often leads to a great change from the original appearance Likewise, in the pyramidal cells of the cerebral cortex the process of shrinkage often leads to a clearly evident change in form

In many types of nerve cells the question of whether there is a decrease in size during the process of aging is a difficult one to settle and few really quantitative studies have been done The complicated shape of the cells, as in the case of the large motor cell

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ate and often appears to be a more or less acute process, or even to be brought about by the actions of the satellite neuroglia cells

In many places change in size of the cells in the nervous system may be evidenced by an increase in the size of the pericellular lymphatic space, the cell which was or

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cases as, for instance, in the inferior olive of the medulla oblongata and in the dentate nucleus of the cerebellum, the pericellular spaces in old individuals particularly are so large and constant as to

occupied them

Decrease in size is not the only size change which may be

degenerative process, they may cause an actual increase in the size of the cell body or of parts of it (fig XI 4) Such is true in the case of the accumulation and increase in size of droplets of fat in certain ganglion cells Such also seems to be the case in some instances of accumulation of pigment This of course, is no more an increase in the actual living substance of the cell than is the increase in size of an undifferentiated mesenchyme cell as it develops fat droplets, as they coalesce, and as the huge single droplet of fat gradually is developed within the substance of the cell

Shrinkage of the cell then, which generally is more clear

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It is natural that a number of investigators should have given attention to the question as to whether or not age changes are seen in the nerve cells in man. Indeed, several papers had described changes as of a disintegrative and atrophic nature before the beginning of the present century. Among these were Hodge (30) and Robertson and Orr (13). In more recent times Andrew (3) and Andrew and Cardwell (13) have described degenerative changes of Purkinje cells and cells of the cerebral cortex in old age in the human subject. Truex (53) has shown a very definite process of degeneration and loss of cells in the human trigeminal ganglion with advancing age.

Riese (41) found considerable destruction in a group of brains from 18 subjects ranging from 77 to 107 years of age, but these were mental cases. Kuhlenbeck (33) has found degenerative changes throughout the cerebral cortex of the rat, the changes being very similar to those which have been described for man. Rothschild (44) described his findings in 21 cases of individuals 60 years to 100 years old at the time of death. Again he dealt with subjects with senile psychoses. He did find widespread alterations in nerve cells in the cerebral cortex in all cases and some decrease in number.

Kuntz (34) described changes in the autonomic ganglia which are primarily degenerative in nature and include in their end stages actual loss of individual cells, together with some increase in the amount of interstitial tissue in the ganglion. *He pointed out that the same types of change which he describes are seen also in many pathologic conditions.* Kuntz and Sulkin (35, 36) stressed the role which the satellite cells play in some of the degenerative processes in the autonomic ganglia.

Of great interest are the findings on degenerative changes in the nerve cells of various parts of the human brain by Oskar and Cecile Vogt (55). These workers and their disciples in more recent years have contributed a large amount of entirely new information in this field of which we shall have more to say later in this paper. It has been my privilege to spend some time in the laboratory of the Vogts and to see at first hand some of the evi*dence for their conclusions.*

Having listed here the names of some of the major contributors of the studies on degenerative changes of nerve cells in lower animals and in man we may turn now to the details of the actual changes themselves.

CHANGE IN SIZE, CELL OUTLINE, AND RELATIONSHIP TO SATELLITE CELLS

The term commonly used in referring to the change in size which comes about in the nerve cell body with advancing age in many parts of the nervous system is "shrinkage." Frequently this is manifested in a conspicuous and striking way. Thus where the normal or "young form" of the cell is well known and characteristic, as for example in the case of the Purkinje



Fig XI 4 Large ... human subject n... of p gment wh ch ... Professor Oskar ... (Courtesy of

DEGENERATIVE CHANGES IN THE NUCLEUS OF THE NEURON

We may now consider the nucleus of the nerve cell during the aging process Our own stud es (see above) had shown nuclear differences be tween young and old animals which while they were not universally pres

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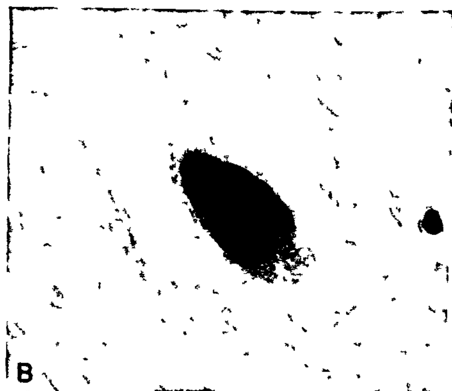


Fig XI 3 *A* cell from the dentate nucleus of a 29 year-old man The cell body is large nucleus and nucleolus clearly seen At this age pigment is present in moderate amounts in some of the cells *B* cell from the dentate nucleus of a 78 year old woman The cell body is small the nucleus obscured and a large accumulation of pigment appearing here as a mass of vacuoles is present at one end of the cell Cresyl violet × 149[illegible]



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DEGENERATIVE CHANGES IN THE NUCLEUS OF THE NEURON

We may now consider the nucleus of the nerve cell during the aging process Our own studies (see above) had shown nuclear differences be tween young and old animals which, while they were not universally pres

ent still were criteria of aging in a good general sense Thus it was noted in the Purkinje cells and in the pyramidal cells of the cerebral cortex and also in the ganglion cells from the trigeminal ganglion that whereas the differentiation of the nucleus from the cytoplasm seen at low power is very sharp in the young animals it becomes increasingly less so with advancing age and in senile animals the borderline is often difficult to make out at lesser magnifications Extension of these studies to the tissues of human subjects showed a similar difference but the exceptions were more marked for instance in the cerebellum and to some extent in the cerebral cortex of individual aged human subjects we have seen many cells with very clear vesicular nuclei standing out well from the general cytoplasm Nevertheless as a generalization concerning change of the nucleus with age the statement of this decrease in differentiation between nucleus and cytoplasm holds true It is due actually to two factors 1) the general decrease in the *amount of Nissl material in the cytoplasm and 2) a tendency to a greater* basophilia of the nuclear sap in the nucleus in the senile nerve cell The nucleolus in the nucleus of the nerve cell generally is paler in the old animal and sometimes shows interesting changes some of which may be degenerative or signs of exhaustion and others which may indicate as we shall mention later *reactive* defensive changes

Since many nerve cells are in process of degeneration we may expect to find nuclei in various stages of actual death and dissolution As long ago as 1911 Dolley described in senile dogs cells which seem to lack a nucleolus or even an entire nucleus such cells being extremely distorted and staining atypically In regard to size there are no consistent figures for the relationship of the nucleus to the cell body with advancing age General observations would indicate that in many cells it is smaller in the old animal than in younger animals for any given group of cell In others again perhaps as a reactive process it may be unusually large

The shape of the nucleus in the senile nerve cell is more frequently atypical in the sense of being elongated somewhat irregular or angular in outline and occasionally lobated Again there are many cells in which the well rounded shape of the nucleus is retained

In old age the position of the nucleus within the cell may be greatly altered This seems to be due however not to any intrinsic tendency of the nucleus to shift position but rather to the accumulation of the inert materials in the cytoplasm Thus accumulations of pigment in the apical portion of the cell may force its nucleus farther toward the basal portion while accumulations in the basal portion will force a centrally located nucleus apically This is true especially in the case of the pyramidal cells In the case of the accumulation of vacuoles of fat as shown clearly in the trigeminal ganglion the nucleus is gradually pushed off far to one side just as in the

case of the development of a fat cell Here, of course, the nucleus also is distorted in shape and may be last seen as a crescent shaped body

CHANGES IN THE CYTOPLASM AND ITS CONSTITUENTS

Turning now to the cytoplasm of the senile nerve cell one of the cytoplasmic components which long has been recognized as of great importance in the nerve cell is the Nissl material The striking changes which this material undergoes under various physiologic and pathologic conditions has made it serve as a good criterion of the condition of the neuron As we all know, in conditions such as poliomyelitis and other neurologic diseases, the Nissl substance may almost or entirely disappear from the body of the nerve cell On section of the nerve, cutting the axones of a particular group of nerve cells there often is clear-cut chromatolysis or dissolution of this material

stance in many of the neurons of older animals This is the type of change which does not seem to be specific for a particular group of cells but which appears to be widespread or even universal in the nervous system, both central and peripheral

It is a striking change, since in many of the cells in youth, as in the large motor cells of the spinal cord in the Purkinje cells or in the pyramidal cells of the cerebral *cortex, the Nissl* flakes are so conspicuous (fig XI 5) In senile animals cells of this type may be almost completely lacking in Nissl substance On the other hand there will always be *some* which have retained a fairly large amount of Nissl material According to our observations Nissl flakes may be retained in approximately the same size and architectural pattern as in youth in some cell

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recent findings with the electron microscope on the fine structure of the neuron Palay and Palade *are of the* opinion and show convincing evidence for their view that the Nissl substance is composed of at least

that structure of the flakes could be maintained while the basophilic component the *extremely* minute granules scattered in the second component a system of fine canals were decreased in amount

The relationship between the *amount* of Nissl material and the presence of inert substances—for we cannot think of the Nissl material as being inert—is of interest In *general* the amount of Nissl material seems to decrease as the pigment increases On the other hand cells may be seen in

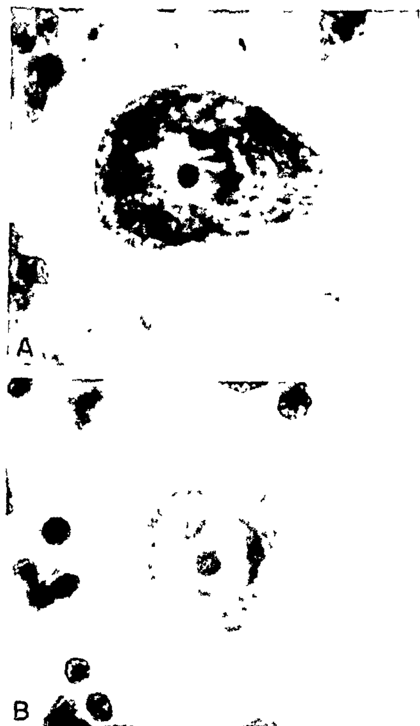


Fig XI 5 *A* Purkinje cell of a 53 year old man showing a great abundance of deeply staining Nissl substance *B* Purkinje cell of a 78 year old woman with well rounded outline but scanty Nissl substance Note that the small nuclei in the vicinity are as deeply stained in *B* as in *A* Cresyl violet × 1195

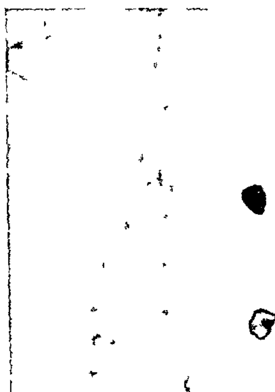


Fig X
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which there is a large accumulation of pigment in one portion with well preserved Nissl granules in the other portion In such cells however Nissl granules are decreased in total number

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the way from a relatively light golden brown through various shades of brown toward dark brown and indeed sometimes almost black in appearance As is well known there are certain groups of nerve cells which contain a pigment throughout all or almost all of the postnatal

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Fig. XI 7 Cell of the substantia nigra of a 41 year old man In these cells where melanin pigment is present in large quantities in young subjects and does not represent a phenomenon of age the Nissl bodies appear as abundant, long and deeply staining flakes (Cresyl violet × 119)

Histochemical studies on the human autonomic ganglion cells by Dr Norman Sulkin in our department tend to confirm earlier observations on the difference in the nature of the aging pigment from the pigment found in these localized groupings of cells The pigment of senescence does not give the reactions which are typical of melanin, such for instance, as the bleaching by strong oxidizing agents such as potassium permanganate, hydrogen peroxide and sodium hydroxide Rather, the age pigment is resistant to this type of change A number of other histochemical tests also serve to distinguish the two pigments It may be pointed out, however, that Levi (37) states that lipofuscin, like all lipochrome pigments, consists of a nucleus of melanin surrounded by a lipoid component, so that some genetic relationship between these pigments is at least conceivable

What, then, is the nature of the pigment which appears in increasing amounts in the cells of many parts of the nervous system with advancing age? The best evidence at present is that it is of the nature of a ceroid, similar to the insoluble pigment which is found in cirrhotic livers While this pigment generally appears in the form of granules, it has been our experience to see it also in what appear to be vacuolar formations In fact, as we shall see later, the amount, appearance, and distribution of the pigment

vary according to the specific type of nerve cell at any given age, at least in man

The accumulation of lipofuscin pigment in nerve cells like many of the other changes which we are describing as occurring with advancing age, are not to be thought of as *specific* changes In other words pigment accumulation can and probably does occur in a variety of conditions other than that of old age and in fact such accumulation is one of the common non specific changes in pathologic states To my mind however, this does not make the gradual accumulation during the aging process any less important for the study of that process particularly as the time of its appearance and the degree of its accumulation seem to be rather constant for special groups of nerve cells even when pathologic conditions do not complicate the picture

I have mentioned the finding of the accumulation of fat in the trigeminal ganglion both in lower mammals and in man Vogt (59) believes that fat can make its appearance in the nucleus and even in the nucleolus of the nerve cell This may of course have to do with its later accumulation in the cytoplasm or such accumulation may be independent of the development of fat within the nucleus In any event nerve cells from a number of localities in man may show large vacuoles of fatty material accumulating with advancing age Thus among the large pyramidal cells there are always some of these cells degenerating through fatty change in individuals of advanced age While the picture of fatty change with the presence of large frequently coalescing vacuoles is quite different from that of the accumulation of the lipofuscin pigment there may well be some definite connection between the two which has not yet been elucidated In fact accumulation of fat in the nerve cell is one of the more conspicuous of the degenerative changes According to Vogt and his disciples (see particularly Buttlar Brentano (21) certain groups of cells in the hypothalamus never show true fatty degeneration but do show lipofuscin accumulation (Nu cle s t ho [illegible]

[illegible] which like the Nissl material is specific for the nerve cell is the neurofibrillar complex Many of the early investigators on nerve cells had described fine fibrils coursing through the cytoplasm of the cell They have been described in cells of many invertebrates of vertebrates and of man Nevertheless in recent times [illegible]

[illegible] learn that Palay and Palade (40) believe that they have seen with very high resolution with this type of instrument struc

tures in the cytoplasm of the neuron which probably represent the neurofibrils of classical cytology

The type of neurofibrillary change known as Alzheimer s disease originally was supposed to be related only to presenile dementia but later indications are that it is fairly widespread in senile brains of human beings in general It consists in an hypertrophy and complication of the pattern of the neurofibrillae often with formation of whorls and baskets of these elements Sosa (18) recently has made a study of the deposition of lipochrome (lipofuscin) pigment and correlated it with a peculiar change in the neurofibrillae which he describes as neurofibrillar degeneration This degenerative process involves a dissociation and agglutination of neurofibrils and ends with a total dissolution of these elements The course of the change runs parallel with the accumulation of the lipofuscin pigment

Turning to some of the elements which are common to all or almost all cells we find that studies have been made upon the Golgi apparatus and mitochondria of the nerve cell with advancing age but that such studies are up to the present very few in number Andrew (4) found the Golgi apparatus in the Purkinje cells of young mice to occur as a large well developed reticular structure composed of coarse threads while in senile animals it was represented by a mass of argentophilic granules of varying shapes and sizes distributed irregularly in the cell The susceptibility of the Golgi apparatus to change was shown in experimental studies by Sulkin and Kuntz (52) in which the reticular structure was altered to a granular one as a result of long electrical stimulation and by induced hypertension This work was done on the cells of autonomic ganglia Not only did the apparatus become granular in many cells but in many others it seemed to vanish entirely

A great deal of attention has been paid recently to the mitochondria in various types of cells particularly since the discovery that associated with these tiny elements are many of the enzymes important in the economy of the cell Mitochondria of the nerve cell however have been a somewhat vexed problem partly on account of the difficulty of the technical procedures to demonstrate them In fact for a number of years during the beginning of the present century there was considerable doubt in the minds of many investigators as to whether or not the nerve cells in adult animals possessed such elements Recently several papers have appeared concerning the mitochondria of the nerve cell in relation to age Hess and Lansing (29) studied the spinal ganglion cells in a group of guinea pigs ranging from new born to senile Their work was done with the electron microscope They found some mitochondria which seemed to be degenerating at all ages examined and concluded that the condition of the mitochondria does not serve as a good criterion of the stage of the aging process in nerve cells Andrew (9 11) has studied the nerve cells from several regions of the cen

tral nervous system, including the Purkinje cells of the cerebellum, the pyramidal cells of the cerebral cortex and the large motor cells of the ventral horn of the spinal cord in the mouse, using pedigreed animals of the C-57 Black stock Our findings include a fairly consistent type of change from a predominence in the younger animals of the long filamentous or long rod like type of mitochondrion in these three types of cells toward a short rod and granular type, frequently even spheroidal or bead like form, in the cells of the senile mice (figs XI 8 and XI 9) These studies are continuing



Fig XI 8 Purkinje cell of a young male mouse of the C-57 Black strain age 6–10 months The cytoplasm shows long filamentous mitochondria together with some thicker rods The molecular layer is above and to the left the granular layer with its mitochondria rich glomeruli below and to the right Regaud's fixation acid *fuchsin stain* × 1670

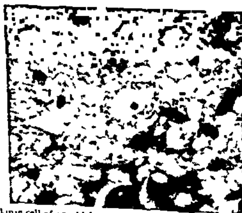


Fig XI 9 Purkinje cell of an old female m

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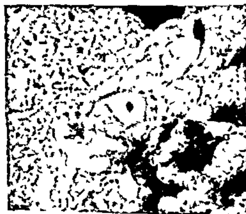


Fig XI 8 Purkinje cell of a young male mouse of the C57 Black stra[illegible]

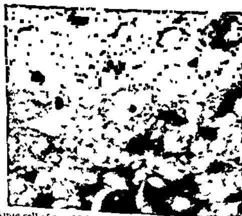


Fig XI 9 Purkinje cell of an old female mouse of the C57 Black strain age 19 months The mitochondria appear chiefly as short rods and granules although some filaments are present. Preparation of specimen and orientation of layers as in preceding figure × 1260

We have discussed the salient changes which have been seen by various investigators in relation to the size shape and outline of the nerve cell body in relation to the characteristics of the nucleus and nucleolus and in relation to the cytoplasm and its various components including Nissl material pigment fat neurofibrillae Golgi apparatus and mitochondria We turn now to a consideration of the processes of the nerve cell the elongated extensions of its cytoplasm which we know as the dendrites and the axones It will be recalled that of these the axon is the more specialized and that the dendrites partake more of the characteristics of the cell body Nissl material and even Golgi apparatus extend part way out into the dendrites Mitochondria on the other hand are found both in the axon and dendrites

In regard to quantitative studies on the numbers of axons or actually the number of nerve fibers in given nerves or nerve roots some of the same difficulties occur as in relation to the quantitative studies on the number of nerve cells at different ages Corbin and Gardner (23) have shown a decrease in the number of dorsal root fibers with advancing age after the third decade in man

There appears to be an increasing complexity of form with the appearance of new processes *i e* short dendrites scattered over many parts of the surface of the cell with increasing age This to begin with is not a senile phenomenon since it may begin fairly early in life Conti (22) has shown that in the sympathetic ganglion cells of the heart this complication in form occurs in early adult life while after fifty years it seems to cease and in fact there appears to be a slight regression in volume of the cell and in richness of the processes in old age A morphologic complication of the nerve cells is reported in the submucous and intermuscular plexuses of Meissner and Auerbach in the gastro intestinal tract of man the process apparently continuing up through middle age according to Borsello and Cavazzani (18) Levi (37) cites a number of Italian workers who have found increasing complexity with age in the processes of cells of the autonomic system In some cases this increasing complexity seems to be correlated with the degree of accumulation of pigment Thus for example in the ciliary ganglion where no pigment accumulates even at a late age the number of prolongations remains constant even in advanced age

In many mammals as in the ox sheep and the goat many polydendritic cells are found in old specimens Such cells have been particularly well demonstrated in the fascia dentata There is a marked new formation of delicate short branches arising from all parts of the surface of the cell body It would seem that at least part of this formation of new processes is concerned with *an increase in the surface of the neuron* which may help to compensate for the poor supply of tissue fluid or blood in the senile animal



Fig XI 10 Aberrant dendrite of a Purkinje cell in a senile mouse a 631 day old male The dendrite proceeding from the small dark cell on the left is seen to be hypertrophied and to contain numerous vacuoles Regaud fixation acid fuchsin stain ×1260

On the other hand according to Truex, cells with aberrant processes in the trigeminal ganglion probably represent degenerate neurons Such atypical cells may be found here in varying numbers at all ages, even in normal ganglia however, they are more common in old age A curious phenomenon of end bulb formation on the ends of certain of the dendritic processes also is seen in senility according to Truex (53) We have seen a thickening and vacuolisation in dendrites of some Purkinje cells in aged mice (fig XI 10)

SPECIFICITY OF THE AGE CHANGES IN PARTICULAR GROUPS OF NERVE CELLS

As we survey the broad general field of the literature on the study of age changes both that which comes to us from the early workers in the field and that which is the product of more recent years of work in this country and abroad, we are impressed not only with the occurrence of a number of changes which appear to be common to all groups of nerve
vancing age
aging an
onset of t ... degree to which the process attains and even in the type of change occurring as a result of senescence in different tribes or species of nerve cells Let us consider a few examples of this phenomenon of specificity by enumeration of the changes which are known to occur in particular groups of cells

In the large motor cells of the ventral horn of the spinal cord *pigment*

accumulation is a noteworthy phenomenon While this pigment accumulation is widespread in the nervous system it does vary considerably in its degree that is in the number of cells involved and in the severity of the involvement of individual cells from one part of the nervous system to another In the large motor cells it has been found by Andrew (8) that there is no pigment in these cells in mice of 10 days of age and pigment in less than 5 per cent of the cells in animals of middle age (312) days In senile mice the accumulation of yellowish brown pigment in the motor cells was conspicuous in every case and indeed the majority of the cells in old animals had half or more of the volume of the cytoplasm filled with pigment while practically every cell showed some of this material This work on experimental animal material is in agreement with earlier work done on human autopsy material by a number of authors including Nonne (39) Sander (16) Huegel (27) and Stern (50) For the rest the motor cells show the general changes which we have described as being common for many cell groups such as decrease in Nissl material change in staining capacity of the nucleus and the nucleolus and the greater frequency of occurrence of satellitosis What we wish to emphasize however is the consistency of the development of the accumulations of the lipofuscin pigment in these cells

In contrast to the motor cells of the spinal cord we may next point to another group of cells which at first thought might be considered as resembling to a fair extent these cells—namely the Purkinje cells of the cerebellum These also are large efferent cells which send out impulses which after relay by other groups of cells reach the skeletal muscles of the body Here however we find a totally different picture in relation to the accumulation of pigment Accumulation of lipofuscin is a very rare phenomenon in the Purkinje cells of the human cerebellum In examining some three score specimens we have seen it definitely in only one instance In the laboratory animal also pigment is very seldom seen in these cells and again we have on record only one animal in which it has been seen out of many specimens and here it was present in only small amounts in individual cells The presence of pigmented Purkinje cells in old age in even a few cases however indicates the tendency which they like so many other nerve cells have to accumulate such pigment It seems only that the tendency is less or perhaps that the resistance of the cell is greater In this relation it is interesting to turn back to an early paper by Dolley (26) In this work he brought about depression in the nerve cells of dogs and rabbits by several methods such as ether anesthesia morphine administration and heat Studies also were made on Purkinje cells the axons of which had been cut In states of profound depression thus brought about experimentally Dolley was able to witness the formation of abnormal pigmentation in the



g XI 11 Binucleate Purkinje cell in a senile mouse a 631-day-old male Each nucleus as its nucleolus Preparation as in Figs XI 8–XI 10 × 2106

rkinje cells Of Dolley's view of the origin of such pigment as from with the nucleus we need to say little The whole question of the origin of gment needs further careful study even at the present time Here then, the motor horn cells and the Purkinje cells we have two species of nerve lls which while they resemble each other in many ways in the processes senescence yet differ radically in respect to the degree of accumulation of ie age pigment

A striking and peculiar phenomenon among the Purkinje cells, which as been described as occurring in old age in mice and rats and in certain pathologic conditions in man is an actual amitotic division of the nucleus fig XI 11) In this process the nucleolus constricts and divides the nucleus becomes horseshoe shaped or dumbbell shaped and then ...
of the n ...
more s
a line ... vision of the nucleus—a formation, as it were of an internal nuclear membrane in the central plane of the nucleus. It has been suggested (10) that this type of amitotic division through an increase in nuclear surface actually is a means of survival of the senile cell We shall see later that some other parts of the nervous system show phenomena similar to this and add further evidence to the intriguing concept of a defense reaction against the phenomena of senescence

A third group of cells those of the dentate nucleus of the cerebellum are

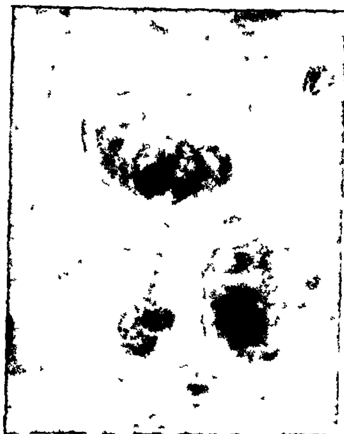


Fig XI 12 Cells of the inferior olive of a 20 year old man The nuclei and nucleoli are well seen Pigment is present in fairly large amounts in cells of the olive even in young persons but the contrast with the same type of cell in a senile person will be seen by comparison with Fig XI 20 Cresyl violet × 149

seen in old age to contain very large accumulations of pigment which seem greatly to have affected the form of the cell and the position of the nucleus (fig XI 8) A recent study by Hopker (91) a student of Oskar Vogt has concentrated on the changes in the dentate nucleus

In the large and conspicuous nucleus of the medulla which we know as the inferior olivary nucleus (fig XI 12) the pigment has a peculiar history It seems to appear almost simultaneously in all the cells of this large nucleus at about the seventh year of life in the human being and thereafter to increase gradually until about thirty years and apparently much more slowly after thirty years This is a striking example of early appearance and very long term accumulation of the age pigment (37)

In the thalamus an interesting relationship is seen among the nuclei in relation to the time of onset and speed of the aging process as evidenced particularly by the actual loss of nerve cells (fig XI 19) The central part

of the thalamus becomes affected earliest Here the nucleus parvocellularis begins to show a loss of cells As the change becomes more marked in it, a similar change begins then in the nucleus mediocellularis and proceeds there Meanwhile the nucleus parafascicularis may be not at all affected as yet, but as the mediocellularis becomes more severely affected, the para fascicularis begins to show change Thus, there is a very clear-cut difference in the onset and rate of aging in these adjoining nuclei of the thalamus

The special areas of the central nervous system which contain cells heavily laden with melanin pigment, namely the substantia nigra and the locus coeruleus also show special types of age changes These consist in a decrease in old age in the amount of the melanin pigment present so that in some cells it is completely lost (fig XI 14) and the appearance within the cyto plasm as the pigment disappears of peculiar 'Masson positive' inclusions often of great size

The nuclei of the hypothalamus show perhaps the most impressive and striking incidence of specificity of age change seen anywhere in the nervous

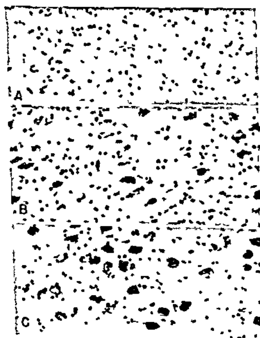


Fig XI 13 Difference in rate of degeneration in nuclei of the ... 82 years old *A* Nuc... mediocellularis mode... Cresyl violet Low po... ... s ... vogt)

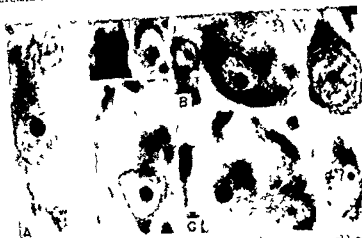


Fig. XI 12. Cells of the inferior olive of a 29 year old man. The nuclei and nucleoli are well seen. Pigment is present in fairly large amounts in cells of the olive even in young persons but the contrast with the same type of cell in a senile person will be seen by comparison with fig. XI 25C. Cresyl violet × 110.

seen in old age to contain very large accumulations of pigment which seem greatly to have affected the form of the cell and the position of the nucleus (fig. XI 8). A recent study by Hopker (31), a student of Oskar Vogt, has concentrated on the changes in the dentate nucleus.

In the large and conspicuous nucleus of the medulla which we know as the inferior olivary nucleus (fig. XI 12) the pigment has a peculiar history. It seems to appear almost simultaneously in all the cells of this large nucleus at about the seventh year of life in the human being and thereafter to increase gradually until about thirty years and apparently much more slowly after thirty years. This is a striking example of early appearance and very long term accumulation of the age pigment (37).

In the thalamus an interesting relationship is seen among the nuclei in relation to the time of onset and speed of the aging process as evidenced particularly by the actual loss of nerve cells (fig. XI 13). The central part



... one as a giant cell the other with a giant nucleus ... a giant and a small cell Cresyl violet Approximately × 600



Fig VI 16 Multinucleate cells from the *supraoptic* nucleus of aged subjects *A* binucleate cells showing differences in the two nuclei *B* binucleate cell in the first two pictures *different* foci of a trinucleate *cell* in the last three pictures *C* a cell with four nuclei shown at *different foci* Approximately × 600

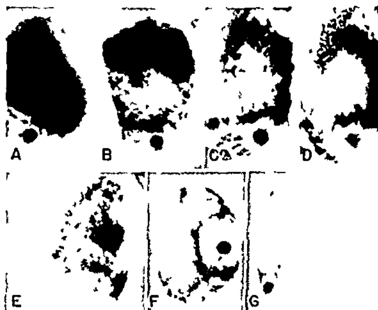


Fig. XI 14. Disappearance with age of the melanin pigment in the locus coeruleus. Progressive steps seen in *A, B, C, D, E, F and G.* Cresyl violet × approximately 600.

system. According to recent findings (21) there is almost no evidence of real degenerative change in the cells of the nucleus supraopticus and of the nucleus paraventricularis.

In these two nuclei of the hypothalamus, Buttlar-Brentano states that she finds no cell destruction (Zelluntergänge) whatever. Also there is no accumulation of lipofuscin in any of the cells nor any other degenerative type of cell change except that in some single nerve cells there is decrease of Nissl material, accompanied by vacuolation, decreasing mass of substance of the cell body and, after a period of hyperchromatosis of the nucleus, apparently a regression of this element. In other words, some indications of cellular degeneration are evident but no evidences of cell destruction. The curious and important finding for these cell groups is the occurrence of certain "reactive" or "defensive" phenomena which seem to have to do with counteraction against the influences which lead on to senescence and ultimate destruction of the nerve cell.

What are these reactive phenomena? They appear to consist in several types of changes in the cell. First, many of the cells of these nuclei in older individuals increase tremendously in size so that they become what may well be called "giant cells" (fig. XI 15) having a surface area of 8 to 10 times the size which these cells have on an average in younger individuals. Second, a number of cells are seen which have two or more nuclei in the cell—multinucleate cells (fig. XI 16)—which by the increased surface area of the nuclei for exchange with the cytoplasm would be in a better position to

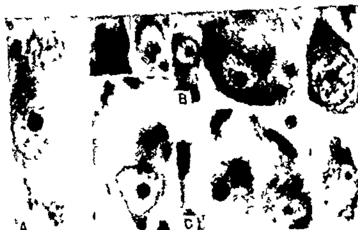


Fig XI 15 Giantism of cells an apparent reactive phenomenon in old age in the supraoptic nucleus A four cells from an 87 year old subject which were in close proximity showing the great variation in size B two cells from an 86 year old subject showing one as a giant cell the other with a "giant" nucleus C two cells in close proximity a giant and a small cell Cresyl violet Approximately × 600



Fig XI 16 Multinucleate cells from the supraoptic nucleus of aged subjects A binucleate cells showing differences in the two nuclei B binucleate cell in the first two pictures different foci of a trinucleate cell in the last three pictures C a cell with four nuclei shown at different foci Approximately × 600

... various cells two three four and even up to six nucleoli (fig XI 17) can be found in a single nucleus Fourth

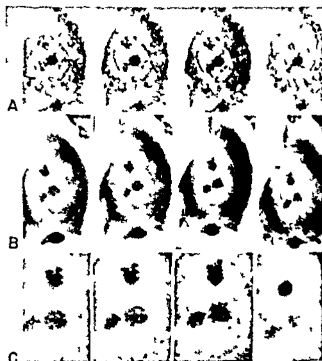


FIG. XI 17. A nerve cell with multiple nucleoli (4) in the supraoptic nucleus of a senile subject. *A*, cell stained with acid fuchsin and light green; the largest nucleolus stained red, the other three green. × 600. *B*, same with cresyl violet stain; all nucleoli staining blue; various foci seen. × 600. *C*, same at × 1200.

there is frequently an increase in the basophilic properties of the nucleus, apparently due to an increase in the amount of ribonucleotide, which can bring the nucleus to a stage which resembles pycnosis but which represents rather, than degeneration, a type of reactive process (fig. XI 18). Buttlar-Brentano had a large amount of good material with which to work, sixty-four brains of individuals from the collection in the Institute for Brain Research of Professor Oskar Vogt. Of the sixty-four specimens, nineteen were from individuals ranging from 77 to 100 years of age.

Recently, in studying the substantia nigra in some senile brain material we have obtained what we consider good evidence of a similar reactive process in cells of this large area. The evidence for reaction here includes a tendency to division of the nucleus (fig. XI 19) and also a tendency to multiplicity of nucleoli which often are of several rather widely differing sizes (fig. XI 20).

In the cells of the higher centers of the brain, in the gray matter which forms the cerebral cortex, as well as in the lower centers, we find definite changes with age (fig. XI 21). Balthasar (11–16) studied particularly the large pyramidal cells in the fifth layer of the Area gigantopyramidalis of



Fig XII8 ... of 83 years ... heavy accum... pigment area ... of the nucleus probably a reactive or compensatory phenomenon Cresyl violet, × approximately 1000 (Courtesy of Professor Oskar Vogt)

the human brain The large pyramidal cells and the giant cells cells of Betz have been divided by Balthasar into two categories namely the centronuclear cells in which the nucleus occupies approximately the center of the cell body and the basonuclear cells in which the nucleus occupies the basal portion of the cell body (fig XI 22) In these two types of cells the location of the accumulating lipofuscin pigment is different In the centronuclear cells it accumulates basal to the nucleus eventually forming a large fairly well circumscribed mass there and tending to move the nucleus toward the apex while in the basonuclear cells it accumulates in the apical portion of the cell tending to move the nucleus eventually basalwards

The zone of cytoplasm in which pigment tends to accumulate has been called by this author the lipophil zone of the cell Accumulation of pigment is a marked feature of the aging process in these pyramidal cells of the cerebral cortex It is pointed out however that the beginnings of this accumulation may be at a fairly early age thus for instance ... age out of 100 ... beginning



Fig. XI 19. Substantia nigra of 78 year old woman. The large cell shows a nucleus of double character, a type of amitosis which is brought about by formation of an internal partition. Cresyl violet × 149



Fig. XI 20. Substantia nigra of 78 year old woman. This cell shows three nucleoli. Multiple nucleoli are very seldom seen in younger individuals. Cresyl violet × 900

18 showed some such pigment in this individual. In 11 centronuclear pyramidal cells only 1 showed pigment, and in 109 basonuclear pyramidal cells 36 showed pigment. In advanced age the pigment-containing centronuclear giant cells showed a ratio of 1.5:1 to the nonpigment-containing; the basonuclear pigment-containing giant cells showed a ratio of 5.1:1 to the nonpigment-containing; the centronuclear pyramidal cells showed a ratio of 2.2:1 to the nonpigment-containing ones and the basonuclear pig



Fig XI 7 General views of motor cortex *A* in a young individual *B* in a senile individual *C* in a case of senile dementia Cresyl violet low magnification (Courtesy of Professor Oskar Vogt)

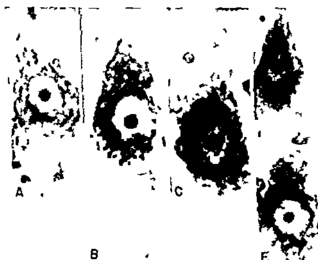


Fig XI 2 Lipopl l f cel ls in large n

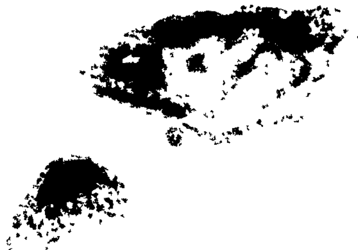


Fig. XI 19. Substantia nigra of 78 year old woman. The large cell shows a nucleus of double character, a type of amitosis which is brought about by formation of an internal partition. Cresyl violet, × 1195



Fig. XI 20. Substantia nigra of 78 year old woman. This cell shows three nucleoli. Multiple nucleoli are very seldom seen in younger individuals. Cresyl violet, × 900

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Fig XI.21 General views of motor cortex *A* in a young individual *B* in a senile individual *C* in a case of senile dementia Cresyl violet low magnification (Courtesy of Professor Oskar Vogt)

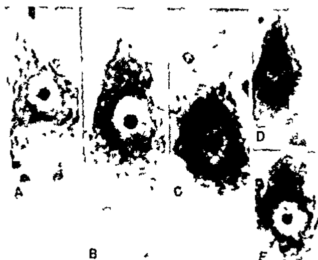


Fig XI.22 [illegible] cells in large pyramidal and giant cells of the two types *A* and *B* centronuclear giant cells *C* [illegible] nuclear giant cell D centronuclear large pyramidal cell *E* basonuclear large pyramidal cell Cresyl violet × 149) (Courtesy of Professor Oskar Vogt)

ment containing pyramidal cells showed a ratio of 1.5 : 1 to the nonpigment containing. While these figures are not based on very large numbers of cell and while they do not deal with the same numbers of cells counted in order to arrive at proportions, the great increase in the numbers of pigment containing cells is readily recognized.

The changes occurring in various areas of the cerebral cortex have been recognized by a number of authors. We ourselves have been struck particularly by the phenomena of increased satellitosis and what appears to be neuronocytolysis of a number of the cells (figs. XI 23 and XI 24). In recent personal observations we have been able to see for the first time also an evidence of a transfer of pigment from the nerve cell body to the satellite cell (fig. XI 25). Our observations agree well in relation to the accumulation of the lipofuscin pigment with the findings by Balthasar.

It is interesting to note that Kuhlenbeck (33) found that increase in lipoid containing pigment is a less prominent feature in the nerve cells of the cerebral cortex in senile rats than in those of senile man, for he witnessed



Fig. XI.23. Two satellite cells (oligodendroglia) deeply indenting dendrite of a large pyramidal cell. 78 year old woman. Cresyl violet. × 900



Fig XI.24 Remains of a nerve cell probably a giant cell of Betz Fragments of cytoplasm and groups of lipofuscin granules are seen with a large number of satellites aiding in the lysis and disposal of this "neuronal debris" 78 year old woman Cresyl violet × 149.

frequent conspicuous accumulation of lipofuscin in the large pyramidal cells in man and very seldom in these same cells in the rat, although he states that spinal and cranial ganglion cells of the aged rat do show a rather marked increase of lipoid and that the nerve cells of the brain stem show some accumulation also Wilcox (60) working with ...
ten ...
sti
mu ... guinea pig

In this regard it is interesting to note that Levi (37) believes that the accumulation of pigment in the nerve cells as well as some of the other changes with age are more marked in the human species than in other mammals

p ...
the
sat ... by Truex (54) and by Truex and Zwemer (55) stands out as a conspicuous phenomenon. More work needs to be done in order to understand how widespread this phenomenon

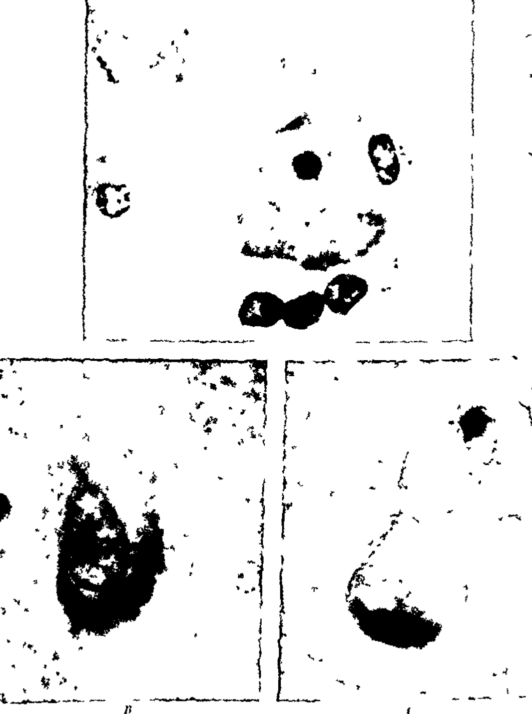


Fig. XI.23. Some aspects of the accumulation of the age pigment, lipofuscin, in human nerve cells. *A*, giant cell of Betz in the motor cortex of a woman of 78 years. Small amounts of pigment are present in the nerve cell but, significantly, one of its *satellites*, that on the right, contains prominent pigment granules. We believe that satellite cells actually remove such material, to some degree at least, from large nerve cells. Cresyl violet. × 1395. *B*, cell of the inferior olive of a 20 year old man. The pigment is scanty in amount. The nucleus and nucleolus are prominent. Masson's stain. × 1115. *C*, cell of the inferior olive in a 78 year old woman. Pigment is abundant and the nucleus is obscured. Masson's stain. × 1110.

is in various of the sensory ganglia and in different species of animals, but the findings in the ganglia which have been examined show a more striking fatty change than has been seen in any other types of cells in the nervous system

In the autonomic ganglia, on the other hand, investigators have failed to find this type of change In fact, the cells of the autonomic ganglia seem to show chiefly the types of age change which we have described for nerve cells in general, the decrease in the Nissl material the deposition of pigment and degenerative changes which frequently lead on to a dissolution of the cell with the occurrence of neuronophagia in moderate degree, brought about by the satellite cells of these neurons, cells which apparently correspond to the oligodendroglia of the central nervous system Neverthe less, the phenomenon of specificity enters here also for in the autonomic nervous system certain ganglia seem to behave differently from others Thus we have already mentioned the fact cited by Levi (37) that the ciliary ganglion seems surprisingly free of pigment even at an advanced age and that, apparently parallel with this lack of pigment, there is a general lack of other types of age change in this ganglion In contrast, the superior cervi cal ganglion is one of the parts of the nervous system which shows the earli est changes of age and which reaches a degree of degeneration attained in few if any other parts of the system

While such differences in the time of onset and the degree of accumula tion of pigment appear to be fairly constant for the different parts of the nervous system, it is certain also that there are individual variations and in some cases the relative times in two parts may even be reversed, as for instance, according to Levi (37) again in the anterior horn of the spinal cord and in the cerebral cortex, where either one or the other may be precocious in the development of pigment Again, there is a report of an individual of 81 years in which all of the neurons of the central and of the peripheral nervous system appear to be free of pigment Unfortunately Levi does not cite a reference for this case, which might be of considerable interest

SUMMARY AND CONCLUSIONS

As is true in so many other fields of scientific effort, the total picture which we now have of the aging process in the nervous system has been the result of the work of a large number of investigators working in many different laboratories and indeed in many countries From their efforts has developed a fairly clear picture of the slow process of change which neurons undergo through the life history of the individual Thus, our picture of aging in the nervous system is based on many well founded ob servations at the present time, and these observations are so numerous

and so confirmatory of one another in many instances that we are able even to do some theorizing about the senescence of nerve cells

The degenerative changes which we have here described particularly for the human nervous system but also applying to other mammalian species such as the mouse rat and the dog present a consistent although somewhat complicated pattern They show both a loss of material such as the Nissl substance and an accumulation of material such as the age pigment They show changes both in the appearance of the cytoplasm and of the nuclei They show a tendency to a change in relationship between the nerve cell and the neighboring neuroglial cells or satellites of the neuron They show in many cases frank degeneration and actual death of cells with their disappearance from the scene They demonstrate also a *specificity* in the aging process in groups of nerve cells in different parts of the nervous system in regard to time of onset severity of change and even type of change which occurs

But now beside this side of the picture of the aging process in the nervous system that of degeneration and death we have attained to a view of an additional aspect of the aging process—one in which we see a certain amount of reaction—of defensive or compensatory change on the part of individual nerve cells In laboratory animals Inukai (32) and Andrew (2 8 10) have demonstrated a process of amitotic division of the nucleus in one type of cell the Purkinje cell of the cerebellum and Andrew (6) and others have shown this process to occur in pathologic conditions in man The extremely important work of Oskar Vogt and his disciples has indicated that a variety of definitely defensive activities occurs in the nuclei of the hypothalamus with advancing age and that these defensive activities are effective in preventing actual degeneration or death of the cells in the supraoptic and paraventricular nuclei It is of immense interest that these reactions include division of nuclei by amitotic division as in the case of the Purkinje cells Nucleolar reaction the division of nucleoli appears also to be a form of defensive activity and makes it seem logical to look closely for phenomena involving the nucleolus when we are considering this type of change in nerve cells It seems probable that the presence or absence of defensive changes in nerve cells will depend in different species upon different factors Surely it appears to be different in the case of the Purkinje cells of man and of the rodent Studies are needed also on many other parts of the nervous system as on the substantia nigra and other areas in which there are some indications of this type of reaction

These new developments in studies on the nervous system should be of great interest and stimulation for further investigations They should make our role as seekers of some means of retarding or ameliorating the aging process seem to be one which is based on firmer ground for now

we can be thought to be acting not only against the degenerative process which is apparently part of the great scheme of nature but also as attempting to aid a process in which the cells themselves are engaged, namely, the defense against the process of degeneration of which we are beginning to see dimly at least some indications in our studies on nerve cells in old age Thus our own efforts will seem to be more in accord with those of nature

DISCUSSION

DR. RAYMOND C TRUEX [Philadelphia Pa] It is a privilege to address this august group and to talk on a subject that has interested me for the last twenty years

This has been an excellent survey of neuronal changes with age by one of the principal investigators in a field of research which is somewhat complex because of the tremendous number of technical difficulties that are involved

Dr Andrew has pointed out that some progress has been made Indeed a great amount of progress has been made by the use of certain morphological techniques as well as histochemical methods We are aware of structural alterations that occur in the nuclei and cytoplasm of the cell including Nissl bodies Golgi apparatus inclusions and mitochondria The most significant changes I think are largely those in the nucleus for many things may happen to the cell in the interval between the time of death and the process of fixation which in itself automatically causes certain morphologic changes However when we add up the total amount of data which we have to date we are aware that we actually have a very meagre amount of quantitative data which will tell us just how much and how great has been the destruction of the nerve cell in any individual part of the nervo is system

Our own stud es during the forties led us to believe that many of the observed ganglion cell changes in the nervous system were secondary to altered blood supply and hen e nor nutrition [illegible]
pendent u [illegible]
al le better [illegible]
of sensory [illegible] By contrast there seemed to be much less degeneration in the structure of the nerve cells of the autonomic ganglia The cells are smaller and there is a trem [illegible]

Dr Andrew has intim [illegible]
he an l his wife in studie [illegible]

[illegible] cell They state that for some [illegible] animal cells with large amounts of storage material in the cytoplasm are more vulnerable and succumb The lethal factor may be too much reserve material inside the cytoplasm of susceptible nerve cells and for too long a time

It is conceivable that the fatty degeneration which we [illegible]
with in ol l age [illegible]
chan cal and [illegible]
aga n ss mer [illegible]
cleus an l [illegible]
of the [illegible]

cells and other parts of the body with age we know so little actually of total values which can tell us of the exact nature and type of such pigmentation

Dr Andrew referred to the supernumerary processes which one sometimes sees in senile neurons It has been stated by many that such bizarre outgrowths of the neurofibrillae may be explained in one of two ways 1) that they represent outgrowths of the cell in an attempt to increase its absorptive surface for gaining of nourishment or 2) that they represent attempts at regeneration on the part of the cell following irritation or injury

Recently we attempted to evaluate these two factors by correlating the postmortem changes on sensory ganglion cells of 19 humans with the known clinical diagnosis Differential cell counts in which we classified 1000 cells per specimen on each of the two sides following neurologic staining were made in cases of severe infection severe burns lues anemia diabetes and alcoholism In each category we failed to find a neuropathologic picture that was characteristic of the given clinical diagnosis Although many atypical cell types were found the normal ganglion cells predominated in each instance

For example in five cases of anemia 89 per cent of the cells were normal whereas in two cases of severe burns 96 per cent of the neurons were normal These findings do not bear out the belief that extraneous outgrowths represent a quest for nourishment as in the case of anemia or a response to irritational damage or toxins to the individual nerve cell as borne out by the case of facial burns I might add here that I am well aware that this is an inadequate sampling

The multinucleation or increased number of nuclei within an individual cell as Dr Andrew has shown us this morning is an interesting and yet unexplained finding It is a common observation in the autonomic nervous system particularly in the pelvic ganglia as was shown by Beaton Holmes and Windle Such cells which often had four or five nuclei were common at all ages and in one instance had nine nuclei We ourselves have seen goodly numbers of such multinucleated cells in the cranial autonomic ganglia of the human newborn In view of the fact that we find such multinucleated cells throughout life I am somewhat hesitant to designate these cell changes as due to aging or that they may represent a defensive reaction

Two brief comments I believe should be made here on neurological technique Bauch and Wyburn you may recall have recently shown that some nerve cells are extremely f[illegible] malin sensitive Susceptible neurons become hydrated and enlarged during the process of formalin fixation and then undergo shrinkage and become angular and dark when dehydrated through alcohol This could explain some of the decrease in neuron size increased cell angularity and the pericellular spaces which we have also found to be common in our own unperfused human material

Secondly one must also cast a judicious eye at some of the Nissl methods which are used A technician will often overstain the microscopic sections and then differentiate and decolorize in alcohol This decolorization will continue if the dehydration steps are prolonged Thus one can produce some very pale washed out cells To eliminate this technical artifact we now use the gallocyanin method exclusively for with this method one may overstain but one can never decolorize or destain and thus produce such chromatolytic cell changes

It is suggested that we might better begin our neurologic studies of aging with the tissues of the fetus and newborn Such an approach would undoubtedly provide us with a more cumulative appreciation of many of the structural alterations which Dr Andrew has designated as a defensive reaction of the cell against aging

Neuron changes with age probably represent a long term experiment on the part of nature The components of each system of the body are influenced to a greater or less degree by the cellular activities of the other systems of the body Stieglitz has recently

published a provocative little paper which I recommend to you in which he has listed the causative influences of a disease as due to predisposing provoking or perpetuating factors I might point out that all three of these factors may have played a very active role in producing the final morphologic picture of senility in nerve cells

Let us examine the neural elements at all ages to gain reliable quantitative data for as Stieglitz noted the young have had no yesterday while the old have suffered the wear and tear of many yesterdays

If more quantitative morpholog c data be one aim for the continued research in this field certainly the second should be to correlate such changes with the antemortem func t onal reserve of the nervous system or a given group of neurons More precise instru

Such a neurological inventory can best be obtained through an interdisciplinary ap proach Here particularly we need an approach that utilizes the combined methods of neuroanatomy physiology biochemistry pharmacology pathology and all the clinical subjects Until such anatomic and physiologic correlation is at hand we can only philoso phize on such basic questions as the following Are different cell groups of the nervous system endowed with a more remarkable compensatory mechanism than others? Does the observed nerve cell destruction with age represent only a partial loss of nature s surplus neural elements that may have been present at birth?

WILLIAM F WINDLE [Bethesda Md] Our present concept of age changes in the br n is clouded

conf

char

the ... that nerve cells may comprise little more than 4 per cent of all cells of the cerebrum

I shall not deal with effects of d sease Postmortem changes are visible in nerve cells one half hour after death and by three hours the cells show rather marked alterations includ ng loss of basophilia and vacuolization of the cytoplasm—alterations which some writers have ascribed to ag ng Because the commonly used fixing fluids penetrate tissue very slowly immersion of the brain or even pieces of it does not prevent postmortem changes from continuing in the interior

Furthermore immersion fixation in formalin produces shrinkage and hyperchromatosis of neurons throughout very small pieces of brain and at the surface of larger blocks of t ssue A well proven method with which danger of these

cells and other parts of the body with age we know so little, actually of total values which can tell us of the exact nature and type of such pigmentation

Dr Andrew referred to the supernumerary processes which one sometimes sees in senile neurons It has been stated by many that such bizarre outgrowths of the neurofibrillae may be explained in one of two ways 1) that they represent outgrowths of the cell in an attempt to increase its absorptive surface for gaining of nourishment or 2) that they represent attempts at regeneration on the part of the cell following irritation or injury

Recently we attempted to evaluate these two factors by correlating the postmortem changes on sensory ganglion cells of 19 humans with the known clinical diagnosis Differential cell counts in which we classified 1000 cells per specimen on each of the two sides following neurologic staining were made in cases of severe infection severe burns lues anemia diabetes and alcoholism In each category we failed to find a neuropathologic picture that was characteristic of the given clinical diagnosis Although many atypical cell types were found the normal ganglion cells predominated in each instance

For example in five cases of anemia 80 per cent of the cells were normal whereas in two cases of severe burns 96 per cent of the neurons were normal These findings do not bear out the belief that extraneous outgrowths represent a quest for nourishment as in the case of anemia or a response to irritational damage or toxins to the individual nerve cell as borne out by the case of facial burns I might add here that I am well aware that this is an inadequate sampling

The multinucleation or increased number of nuclei within an individual cell as Dr Andrew has shown us this morning is an interesting and yet unexplained finding It is a common observation in the autonomic nervous system particularly in the pelvic ganglia as was shown by Beaton Holmes and Windle Such cells which often had four or five nuclei were common at all ages and in one instance had nine nuclei We ourselves have seen goodly numbers of such multinucleated cells in the cranial autonomic ganglia of the human newborn In view of the fact that we find such multinucleated cells throughout life I am somewhat hesitant to designate these cell changes as due to aging or that they may represent a defensive reaction

Two brief comments I believe should be made here on neurological technique Basch and Wyburn you may recall have recently shown that some nerve cells are extremely formalin sensitive Susceptible neurons become hydrated and enlarged during the process of formalin fixation and then undergo shrinkage and become angular and dark when dehydrated through alcohol This could explain some of the decrease in neuron size increased cell angularity and the pericellular spaces which we have also found to be common in our own unperfused human material

Secondly one must also cast a judicious eye at some of the Nissl methods which are used A technician will often overstain the microscopic sections and then differentiate and decolorize in alcohol This decolorization will continue if the dehydration steps are prolonged Thus one can produce some very pale washed-out cells To eliminate this technical artifact we now use the gallocyanin method exclusively for with this method one may overstain but one can never decolorize or destain and thus produce such chromatolytic cell changes

It is suggested that we might better begin our neurologic studies of aging with the tissues of the fetus and newborn Such an approach would undoubtedly provide us with a more cumulative appreciation of many of the structural alterations which Dr Andrew has designated as a defensive reaction of the cell against aging

Neuron changes with age probably represent a long term experiment on the part of nature The components of each system of the body are influenced to a greater or less degree by the cellular activities of the other systems of the body Stieglitz has recently

people like Charles Darwin and Einstein Newton and others did involve some philoso phizing

It is true that there is only a partial loss of nerve cells, and it is difficult to say just what this means in terms of function in different parts of the nervous system

In regard to Dr Windle s very interesting comments I think that the picture of the nerve cells as seen after perfusion fixation of the material which was studied certainly presents a more optimistic future for the guinea pig in relation to old age than the ma jority of students of the human brain have found for man These were animals from a very well kept laboratory the laboratory of Dr Rogers at Louisville Certainly, the per fusion method is a most interesting one I have felt sometimes in cases of study by means of perfusion that there should be controls, using the material from the same or similar animal by immersion technique in each case In any event, of course, it is difficult to hope to obtain any large amounts of human material fixed by means of perfusion of the nerv- ous system

Certainly, it is true that some changes were seen even with such fixation and Dr Windle remarks that the only striking' difference was the accumulation of pigment, per haps implying that there were some other differences

With regard to the degree of satellitosis at different ages, that question is still somewhat unsettled. Surely in the human brain the impression has been that satellitosis increases with advancing age Of course we are dealing here with a very complicated situation We are dealing with human beings who have died from various conditions and with varying clinical pictures We have tried to present this paper in the form of a survey of what has been learned what has been concluded from a study of a very large amount of material There is no way to prove that changes at the present time are due to purely "physiologic aging What we are talking about are changes that occur in old age or changes that are visible in old age and not in the younger age groups

With regard to the important question by Dr Merritt concerning the other portions of the *nervous system* besides the nerve cell, some studies have been made There have been recent findings by Dr Kuhlenbeck at Woman s Medical College of changes in the sciatic nerve with degeneration of some of the fibers in old age and the appearance of large phagocytic cells within this nerve Studies on the astrocytes the microglia, and the oligodendroglia are difficult to make It is hard to be sure that one has an effective tech nique in making *these studies* But there are some early reports of age changes in the glial cells by some of the Spanish histologists of the Cajal school

With regard to the nature and the reality of these changes, some, of course are open to definite criticism and question *others it seems to me* are rather difficult to set aside as being due to difference between types of fixation or other techniques For instance, one hardly can feel that the use of one fixation technique rather than another would lead to the presence of fat in cert[illegible]

that amyloid bodies would app[illegible]

One hardly can feel that one [illegible]

which [illegible]

of fixa[illegible]

hardly [illegible]

In r[illegible]

a lequ[illegible]

made [illegible]

terned [illegible]

a the [illegible]

Th[illegible]

cells [illegible]

[illegible] any years ago, back in 1911 to

In conclusion I want to sound a note of caution in interpretation of results obtained by uncontrollable histopathological techniques When methods are properly applied to avoid postmortem and fixation artifacts surprisingly little in the way of age changes can be detected in healthy animals nerve cells

DR H HOUSTON MERRITT [New York N Y] I would like to ask Dr Andrew how extensive a study has been made of other elements of the nervous system to determine if they are an index of the aging process particularly the glia the blood vessels and the myelin sheaths

RAYMOND ADAMS [Boston Mass] Dr Merritt has already asked my question but I would add to his list the amyloid bodies that are found in the aging nervous system I too would certainly follow the line of thinking that Dr Windle has presented I have seen some of Dr Vogt s material and felt that there had not been ample control of post mortem change fixation artifact and things of that sort The question then of how many of these very subtle changes in the neurons are reliable indices of disease must always be kept in mind

There is another problem however Assuming that these changes are reliable what do they mean? What do they mean in terms of reactivity to some disease process or compensation to a disease process? How does one decide whether a cell change is compensatory? That is a question that deserves comment And then assuming that you can decide that question how do we determine that these changes are specifically related to the process of aging inasmuch as every animal and every human has been assailed by an endless series of diseases and metabolic changes? That is one of the vexing problems in this whole field and I frankly admit that I am confused about it

DR WILLIAM MALAMUD [Boston Mass] I would like to continue the question that Dr Adams raised and particularly ask how much do we know about the clinical picture of the people whose brains were examined? With the 500 brains that Dr Vogt has and 25 000 sections in each brain how much clinical material does he have? If he doesn t—well I feel it is just too bad to have Dr Lorge yesterday telling us about very minute studies of the psychologic picture and Dr Andrew and Dr Truex telling us about the histologic changes and yet no attempt made to bring them together

DR AUGUSTUS ROSE [Los Angeles Cal] I would like to ask how the morphological changes described by Dr Andrew relate to those shown many years ago by Dolley in the Purkinje cells of the dog s cerebellum?

DR WARREN ANDREW In regard to the discussion by Dr Truex the point is very important that multinucleation of cells does occur in certain parts of the nervous system at all ages and this is well recognized It again points up the fact that we must talk about individual groups of cells rather than about nerve cells in discussing some of these age changes As a matter of fact in the nuclei of the hypothalamus we do have multinuclear

functional significance of these changes and that the use of the combined disciplines is highly to be desired in such studies

There is necessarily a certain amount of philosophy and philosophizing bound in with our present views on aging of nerve cells and this may be a bad feature but in many fields of science philosophizing is of extreme importance and of course the work of

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1917 Frankly I have always thought a great deal more of Dr Dolley s work than many of his critics have His studies were made by methods which some of us feel are a bit antiquated today but he had beautiful pictures of changes in Purkinje cells as a result of normal senescence and of fatigue and actually there has been a fair amount of correlation of our own findings with the findings by Dr Dolley on the dog

I do feel that the truth in this question of the degree of change in nerve cells in old age probably lies somewhere between the stand which some investigators and I have taken that there is a fairly large amount of change in nerve cells and the findings by Doctor Windle with the perfusion techniques that there is relatively little change I certainly do not think that this is an all or none question and only the future will decide which of the present views is the *more* correct one

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CHAPTER XII

HYPERTENSIVE AND ARTERIOSCLEROTIC VASCULAR DISEASE OF THE BRAIN IN THE ELDERLY

JOSEPH M FOLEY

However the word elderly may be defined the result is arbitrary, and therefore unsatisfactory In this study the biblical age of three score and ten is the arbitrary choice since there are enough patients surviving above the age of 70 to give some meaning to certain numerical data which will be presented Eleazar s four score and ten and Job s one hundred and forty years are almost equally famous but obviously impractical for present purposes

The poet the philosopher and even the biologist will not be satisfied with this chronologically determined definition but none of them has provided the criteria for any other The old saw that a man is as old as his blood vessels has only an incomplete justification A youthful set of blood vessels may be providing nutrition to a very degenerated set of nerve cells so that functionally the man is old in awareness and responsiveness and will never regain the physical or mental attributes of youth We are old or young only in quantitative terms of our awareness and our responsiveness When the definition as here is chronologic, the emphasis is on the actuarial feature of life expectancy

Arteriosclerosis is defined as a degenerative change in arteries of any [illegible]

[illegible] and with or without atheromatous change in blood vessels These definitions will be to some as arbitrary as the definition of elderly but they are necessary to limit the scope of the discussion The elderly patient with arteriosclerosis or hypertension almost always has some degree of *structural* change in the cerebral blood vessels Arteriosclerotic or hypertensive vascular disease of the brain is considered to be the effect of these degenerative processes upon brain tissue in terms of either loss of nervous function or destruction of nervous tissue

The patient who has survived for three score and ten has had seventy years of opportunity for challenge by trauma infection neoplasia and metabolic error But as he outruns these pursuers he is headed off by the

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These changes and their effects upon the brain will be considered in more detail when lacunar infarcts are discussed The larger blood vessels at the base of the brain may not be affected by hypertension and it is not un common to see normal vessels in the circle of Willis when the hypertension has been severe enough to cause a fatal ganglionic hemorrhage When atherosclerosis is present in the circle of Willis hypertension may potenti ate the degenerative effect of the atheroma with the production of aneu rysmal malformations

For all practical purposes the effect of arteriosclerotic vascular disease upon the brain is infarct necrosis Conversely, almost all instances of in farct necrosis of the brain in the elderly are related to arteriosclerotic vascu lar disease since so-called cerebral thrombi arise in arteriosclerotic cere- bral vessels and cerebral emboli arise in arteriosclerotic hearts or great vessels Further the extent of the destructive effects of thrombi or emboli in cerebral vessels is conditioned strongly by the relative patency of other cerebral vessels which in turn is a function of the extent of arteriosclerotic degeneration which they have sustained

Atherosclerosis of the basal vessels of the brain can sometimes reach such a magnitude even when not aneurysmal that compression of cranial nerves may occur with visible flattenings and indentations It is sur prising how infrequently a loss of function can be documented in such cases especially in those cases in which the optic nerve and chiasm are compressed (8) Presumably the slow development of the compression and distortion allows the nerve fibers to adapt

In recent years there has been understandable impatience with what has been called the plug and spasm school of thought in cerebral infarction Denny Brown (9) has proposed the term hemodynamic crisis

... insufficiency, and Millikan and his co workers (11) have been referring to acute intermittent insufficiency of cerebral vessels

The hemodynamic crisis in one form or another precedes all infarction in the sense that there is a time interval in which dysfunction of tissue is still reversible It is well known that an area of brain deprived completely of blood for more than a few minutes will undergo irreversible necrosis It is less well known that incomplete degrees of perf...

...taneous event in ... there may be som... ...of some residual oxygen in blood

degenerative diseases The big challenge of the degenerative diseases of later life is to the blood vessels Most feared and most disabling is the threat to the vessels of the brain for when dementia or paralysis takes over a man can no longer control his own destiny Old people do not fear death as much as they dread the steps leading to it (1)

Several reviews and symposia in recent years have concerned themselves with the nature and etiology of arteriosclerosis and hypertension Great strides have been made in our knowledge but therapy is still in the experimental stage even though some approaches seem more reasonable than others (2 3) No preventive and no cure for degenerative vascular disease of the brain is in the foreseeable future and a large task remains in trying to learn the mechanisms by which hypertension and arteriosclerosis exert their effects on brain tissue An excellent critical review of cerebrovascular disease with emphasis on recent practical additions to clinical and pathological features was published in 1953 (4)

Hypertension may affect brain tissue in a variety of ways The most dramatic and violent of its manifestations is hemorrhage into brain substance Indeed brain hemorrhage in the absence of malformation trauma or blood dyscrasia is invariably due to severe and long standing hypertensive vascular disease The mechanism of rupture is still unknown Charcot s miliary aneurysms are no longer considered to be an adequate cause (5) No more convincing as a cause is the artificial situation of experimental infarction preceding acute rise in blood pressure (6) Although some few human cases may correspond to this experimental situation the lesions are more reminiscent of severe hemorrhagic infarction than true brain hemorrhage

Hypertensive encephalopathy is a crisis in the course of hypertensive disease in which headache coma convulsions eyeground changes and varying degrees of renal failure make their appearance in a patient whose already high blood pressure has gone up acutely The pathologic lesions in the brain consist largely of swelling miliary infarcts petechial hemorrhages and evidence of increased vascular permeability superimposed upon more chronic vascular lesions The presumption is that this crisis in the course of the disease is due to an acute increase in intraluminal pressure (7) involving not only the cerebral but the visceral vessels as well Hypertensive encephalopathy is very rare in the elderly The reason for this is not clear It is not only that the severe hypertensives die earlier since we shall see that cerebral hemorrhage is not infrequent in the older patient

The earliest morphologic change in the brain in hypertension is in the smaller arteries which become thickened by cellular proliferation and then hyalinized In some instances this reaction may become necrotizing

TABLE XII 1

Age distribution of cases

Age	433 Cases Over 70 at Autopsy 53 1 per cent male 46 9 per cent female	334 cases over 70 with Brains Examined 51 4 per cent male, 48 6 per cent female
70-74	31 6 per cent	30 8 per cent
75-79	29 8 per cent	29 0 per cent
80-84	24 7 per cent	25 4 per cent
85-89	9 7 per cent	9 9 per cent
90-94	4 2 per cent	4 5 per cent

Of these 334 cases 131 or 39.2 per cent, had infarct necrosis or hemorrhage attributable to hypertension or arteriosclerosis

TABLE XII.2

Type of lesion in 131 patients with hemorrhage or infarct

Lesion	No	Per cent
Hemorrhage	12	3 6
Infarcts Recent	58	17 4
Infarcts Old	87	25 8
Infarcts Old and Recent	21	6 3
Hemorrhage with Old Infarcts	2	0 6
Hemorrhage with Recent Infarcts	0	—

tion of the brain was carried out in 334, or 77 1 per cent Table XII 1 demonstrates that at least in terms of sex and age this group of 334 cases in which brains were examined is representative of the total in which autopsies were carried out Recent infarcts were present in 58, or 17 4 per cent of the total Table XII 2 Old infarcts without recent lesions were present in 89 or 26 per cent In 21 cases or 6 3 per cent, there were both recent and old infarcts Of the 58 recent infarcts, we have tried to determine how many were the principal cause of death An infarct may be the cause of death because of its size as in cases of massive hemispheral infarction (fig XII 1) or because of its location as in the vertebral basilar distribution (fig XII 2) or because of a functional disability which permits of easy fatal complications Using these criteria there were 40 cases or les [illegible]

[illegible] for 120 deaths (27 9 per cent) and malignant tumors for 90 deaths (20 8 per cent)

That 10 per cent of patients died of a cerebral infarct is of course no index of the morbidity produced Every patient who sustained a cerebral in

vessels in and near the cerebral areas whose integrity is threatened. Necrosis of nervous tissue is brought about by the duration and intensity of the ischemic anoxia. The resolution of the hemodynamic crisis is favorable or unfavorable depending upon the intensity of the anoxia and the speed with which adequate perfusion is restored.

Fixed collaterals are the main line of defense against infarction of brain tissue. When they are anatomically inadequate, as for example in the origin of both anterior cerebral arteries from the internal carotid of one side, an infarct may be disastrous in its extent. But the margin of safety is usually considerable, for not only are there anastomoses in the major vessels of the circle of Willis, but there are other meningeal anastomoses between the branches of these major trunks (12). It is likely that such anastomotic conections are effective if the occlusion of a vessel is sufficiently gradual. In the sudden occlusion produced by embolus there is infarction in the total area of supply of the vessel beyond the point of lodgment of the embolus. But in the gradual occlusion produced by concentric atherosclerotic obliteration or stenosis of a vascular lumen, no infarct may be present under normal circumstances. When occlusion has been gradual, or perhaps even when it is incomplete, the collaterals from other patent vessels take over to protect the area of compromised supply. These collaterals are effective only up to a point. Their failure depends upon several factors, the most important of which are their own relative patency and the effectiveness of the general circulation.

The mechanisms by which collaterals succeed and fail are not understood completely; more information about them will be essential for an understanding of the mechanisms of cerebral infarction.

FREQUENCY

With these preliminary considerations in mind we might now consider the incidence of arteriosclerotic and hypertensive vascular disease of the brain in the elderly patient in our time. To this end we have reviewed the autopsy records of the Mallory Institute of Pathology for the year 1954. It is obvious that there is a degree of selection in such a series. For one thing, the patients are dead. For another, although the population of a City Hospital is generally older than that of other kinds of institutions, it is not as likely to include a large number of chronically demented patients such as might be seen in a similar age group from a mental hospital. On the other hand, autopsies in a City Hospital population are likely to give a rough appraisal of the pathological processes in the general population.

In the year 1954, 1050 autopsies were performed at the Mallory Institute on patients who had died at the Boston City Hospital; 133, or 11.2 per cent, were in patients 70 years of age or older. Of these 133 cases examina



Fig XII ? Extensive infarction of the rostral pons in a 2 year-old woman who died within ? hours of her collapse The right cerebellar hemisphere was also infarcted The lower picture shows the degree of narrowing of the basilar artery below the level of the lesion



Fig XII 1 Massive infarction of the right hemisphere in an 81 year old hypertensive woman due to embolic occlusion of the right internal carotid artery There were bilateral tentorial herniations and mid brain crush Death occurred within 48 hours of the onset of symptoms

farct is disabled to some degree as are many others who are threatened with infarction without sustaining it

Of the 331 cases in which brains were examined 12 hemorrhages were found In all but one the hemorrhage was the cause of death In every one of these cases there was hypertensive heart disease as manifested by heart weight of 400 grams or over In these 331 cases there were 51 instances of hypertensive heart disease so that over one quarter of hypertensive patients died of cerebral hemorrhage in this age group There is apparently no age beyond which hypertension may not produce brain hemorrhage Three of our patients were over 85 and one over 90

This then has been the dark side of the picture, that almost 40 per cent of patients who live to the age of 70 or over will show some effect on their brains of hypertension or arteriosclerosis There is however, a brighter side Not all of these lesions caused death, nor indeed did all produce significant disability And of the 331 cases there were 203 (over 60 per cent) in which no infarct and no hemorrhage occurred The last two columns of table XII 3 show the relative age distribution of the affected and the unaffected groups Except for a lower incidence of involvement in the

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Fig. XII.2 Extensive infarction of the rostral pons in a 72 year old woman who died within 72 hours of her collapse. The right cerebellar hemisphere was also infarcted. The lower picture shows the degree of narrowing of the basilar artery below the level of the lesion.

TABLE XII 3

Age distribution of cases with and without cerebral vascular lesions

Age	At Autopsy (431 Cases)	%	Brains Examined (334 Cases)	%	No Infarct or Hemorrhages (203 Cases)	%	Infarcts or Hemorrhages (131 Cases)	%
70–74	137	31.6	102	30.8	70	34.5	32	24.4
75–79	129	29.8	98	29.0	58	28.6	41	31.3
80–84	10[illegible]	24.7	85	25.4	50	24.6	35	26.7
85–89	42	9.7	33	9.9	19	9.4	14	10.7
90–94	18	4.2	15	4.5	6	2.9	9	6.9

earlier age groups there is no significant difference in age distribution Since we are here analyzing a negative factor the absence of a lesion this figure of 60 per cent may be high but at least it would appear that very many people can attain very advanced years without any striking pathologic changes in their brains which are attributable to hypertension or arteriosclerosis

Another instructive feature to be gained from studying autopsy material relates to the other pathologic states which occur with degenerative vascular disease of the brain Most obvious and probably most important is the state of the rest of the vascular system Arteriosclerotic heart disease in our material is considered to be present when there is coronary artery disease with old or recent myocardial infarction myocardial fibrosis or arteriosclerotic valvular thickening With these criteria arteriosclerotic heart disease was present in 83 per cent of 133 patients over 70 and in 92 per cent of 131 cases in which either infarct or hemorrhage was present in the brain Not all of these cases were symptomatic but in our 133 patients death was due to cardiac failure or myocardial infarction in 28 per cent Monroe (1) has reported on the incidence of heart disease in 7911 patients over 61 in the years 1913–1918 at the Peter Bent Brigham Hospital In this group younger than our own he found clinical heart disease in 55 per cent and at autopsy in 72 per cent

This high incidence of heart disease means that we must direct our attention to the heart in all cases of vascular disease of the brain but especially in the elderly Auricular fibrillation or myocardial infarction with embolic occlusion of a brain vessel is easily recognized Less well recognized are the episodes of sudden neurologic disability consequent upon myocardial infarction coronary insufficiency angina pectoris and changes in cardiac rhythm These events set in motion a chain of circulatory derangements the least complex of which is the blood pressure drop of myocardial infarction The cerebral result of these events in the presence

of stenosis or occlusion of a cerebral vessel is a hemodynamic crisis which may produce localized loss of brain function

Case 1 An 80 year old woman suddenly collapsed at home and became unconscious immediately Within several hours she was brought to the hospital She was pulseless and without blood pressure and died before other observations could be made At autopsy there was found an early myocardial infarct without mural thrombi There was extensive early infarction of the tegmentum of the pons and midbrain the left thalamus and both occipital lobes (fig XII 3) The basilar artery was markedly narrowed by atheroma and contained a newly formed fibrin clot

Case 2 An 88 year old woman had angina pectoris She was admitted following the sudden onset of left hemiplegia with unconsciousness She made a moderately good recovery over the next several days Three days later she was alert oriented and jocular and her hemiplegia was clearing It continued to improve until she died suddenly while eating eleven days after her original collapse She had never complained of chest pain or discomfort At autopsy there was infarction of the anterior wall and the septal portion of the left ventricle considered by histological criteria (13) to be consistent with an eleven day infarct In the brain there was recent incomplete infarction in the distribution of the right middle cerebral artery which was narrowed but not occluded by atherosclerosis (fig XII 4) The very sclerotic right internal carotid artery was occluded at its terminus by a ruptured atheroma(fig XII 5) A reconstruction of the clinical events would suggest that the cerebral lesion was the result of the hemodynamic derangement produced by the acute myocardial infarct in a cerebral vascular system already compromised by atherosclerosis

Such cases as these illustrate that there are mechanisms other than embolic occlusion by which the cardiac events may produce cerebral infarction In the first case the infarction in the basilar distribution was conditioned by the stenosis almost to obliteration of the basilar artery Adequate as this narrowed lumen and its fixed collaterals may have been prior to the myocardial infarction the tissue was unable to survive the diffuse circulatory derangement of a shock producing myocardial infarct The role of the fibrin thrombus was intermediary at most, indeed it may be possible to regard it as only another effect of the local ischemia produced by the myocardial infarct

In the second case the occlusion was in the internal carotid artery, but the infarction was in the distribution of the middle cerebral artery, which was not completely occluded, although it was very stenosed Ruptured atheroma in the cerebral vessels has not been associated previously with hypotension but Mallory and Kinney (14) have reported it in the coronary arteries as a consequence of bleeding peptic ulcer They advanced the hypothesis that rupture occurs as a consequence of the pressure difference produced by the lowered intraluminal pressure

The cardiovascular system is not the onl

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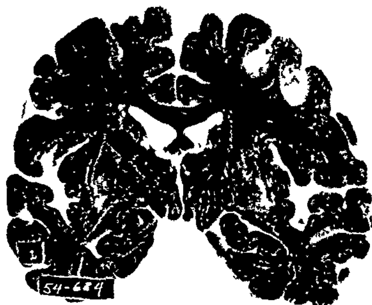


Fig XII 4 Case 2 Incomplete softening in the distribution of the right middle cerebral artery in an 88 year old woman with an 11 day old myocardial infarction

and many others can be cited in our material as precipitating events in cerebral infarction Behind all of these looms the least common denominator of cerebral arteriosclerosis contributing by stenosis to a situation favoring hemodynamic crisis and thwarting by impaired collaterals the success of the adaptive mechanisms which prevent infarction

The diagnosis treatment and prophylaxis of cerebral vascular disease in the elderly demand that we direct our attention not only to the events in the cerebral vessels but to those extracerebral events which produce diffuse circulatory effects We must reject the idea that cerebral infarct or even cerebral thrombosis may arise *de novo* and *sine causa* Documentary evidence regarding hypotension as a cause of the unsatisfactorily resolved hemodynamic crisis is attainable in a certain number of cases but there are many other possible causes of reduced vascular perfusion of a compromised cerebral area which are less readily documented Decreased cardiac output alterations of cardiac rhythm and increased vascular resistance result in reduced cerebral blood flow but in the critical event leading to cerebral infarction their presence often can be only surmised Indeed in acute myocardial infarction the diffuse circulatory derangement is complex and factors other than systemic and cerebral hypotension may be contributory Modern studies in cerebral vascular disease must ask the





Fig XII 3 Case 1 80 year old woman who collapsed suddenly and died within several hours At autopsy there was found an early myocardial infarct without mural thrombi There was early infarction of the tegmentum of pons and midbrain the left thalamus and both occipital lobes

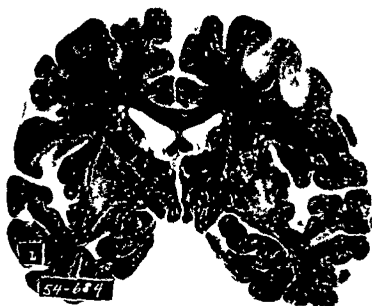


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These lesions have been considered by some to be the anatomic substrate of common motor disorders of the elderly including marche à petit pas and even parkinsonism The severe grades of lacunar degeneration of the lenticular nucleus are very rare in our own material but lesser degrees of change are not uncommon in the elderly patient (fig XII 6)

When the lacunar state is present to any degree in the putamen there usually are lacunar changes elsewhere The griseum pontis the thalamus and the centrum semiovale and other favored sites When this process occurs in younger patients they are almost invariably hypertensive, although some are diabetic We have not seen such change well developed in a younger non-diabetic or non hypertensive and if it occurs it must be extremely rare Lacunar degeneration is a familiar finding however, in the older patient It may occur without hypertension in the aged although hypertension combined with advanced years produces it in its most classical form

The earliest morphologic change in the cerebral blood vessels in hypertension affects the smaller arteries and arterioles Even patients with long standing hypertension may show no significant atheromatous change in larger cerebral vessels In diabetics and in elderly patients with long standing atherosclerotic vascular disease the atherosclerotic process extends



Fig XII 6 Extensive lacunar infarction of the lenticular nuclei in a 90 year-old non hypertensive non diabetic woman



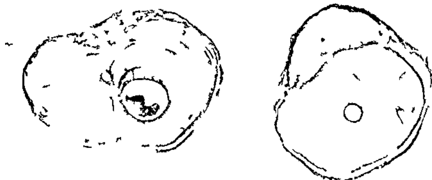


Fig. [illegible]. Case 9. The large vessel is the right internal carotid artery occluded by [illegible] ruptured atheroma. The smaller vessels are branches of the right middle cerebral artery. Their lumens are markedly narrowed by atheroma.

question. Why did this cerebral infarct occur in this patient at this time? Only by a correct answer to this question in large numbers of cases can we hope for an intelligent approach to the prevention of cerebral infarction.

LACUNAR LESIONS

The neuropathologic literature from the middle of the nineteenth century has carried accounts of small lesions in the lenticular nucleus, especially the putamen. Pierre Marie (15) used the term état lacunaire

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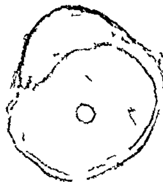


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F g XII.6 Extens e lacunar infarction of the lent cular nuclei in a 90 year-old non hypertens e non-diabet c woman

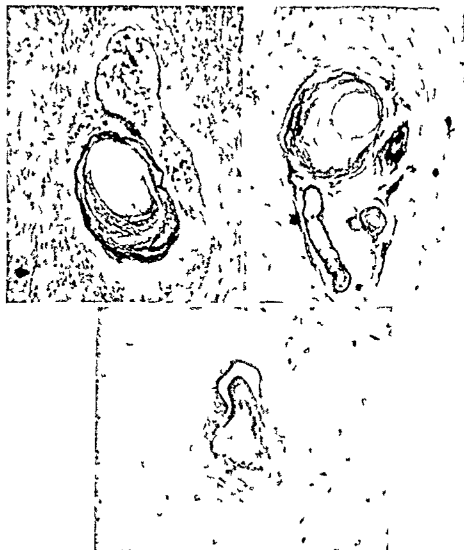


Fig XII 7 Degenerative changes in smaller blood vessels near lacunar infarcts in putamen and pons of a 78 year old hypertensive man The upper two vessels have been stained by Verhoeff s method the lower by hematoxylin and eosin

into the smaller arteries Figure XII 7 illustrates some of these vascular changes in the neighborhood of lacunar degeneration In our view lacunar degeneration is merely the consequence of obliterative vascular disease of the smaller sized arteries and arterioles referred to customarily but not quite accurately as arteriolosclerosis The vulnerability of the putamen is probably due to a combination of its high metabolic demand and the relative poverty of its fixed collaterals

The *état lacunaire* of Pierre Marie is then an effect of degenerative

vascular disease of the brain Alexander (16) regards the *status cribratus* and *precribratus* of the Vogts (17) as lesser degrees of the same change Moore (18) has recently proposed the idea that certain perivascular cavitations seen in the putamen and elsewhere are the effect of a lytic action of certain ferments stimulated by hypoxia

In recent years there has been a widespread uncritical invocation of "little strokes to explain many neurologic and indeed many non neurologic symptoms and signs in patients of all age groups but especially in the elderly (19 20) Neurologists aware of the flimsy nature of the clinicopathologic evidence on which this concept is based have been cynical on the one hand and generous in their unwillingness to criticize on the other As a result the idea of little strokes has attained a widespread popularity among some non neurologic practitioners for whom it represented a plausible explanation of some otherwise obscure clinical problems Thus a patient has a pain in the chest or a drop in blood pressure or a confusional episode or a gradual dementia or a depression and a little stroke is diagnosed

There are such things as little strokes as there are such things as big strokes but the practitioner does his patients a grave disservice when he deceives himself into thinking he has made a diagnosis when he uses the term *little stroke*

The true little stroke is the symptom whatever it may be that results when a patient has had a lacunar infarct In the sense that lacunar infarcts may occur in showers and may be widespread throughout the brain they are frequently the pathologic basis of pseudo-bulbar palsy and dementia When pathologic material is used to illustrate the little stroke notion the lesions are seen to be *lacunar infarcts* and whenever the data are provided the patient is found to be hypertensive (19)

The implication that an individual lacunar infarct can produce all of the symptoms ascribed to it in the *little stroke* idea is untenable and dangerous The notion that every cerebral episode that occurs in the elderly is a vascular thing can find no support from the study of a large number of autopsies In our own material subdural and epidural hematomas and tumors aneurysms and infections of the nervous system turn up with sufficient frequency to provide evidence if any were needed that the neurologically sick elderly patient is entitled to more than the casual assumption of *vascular etiology* that too often represents the total medical analysis of his problem (figs XII 8 and XII 9)

ANEURYSMS

Saccular aneurysms of the cerebral vessels are in our view congenital They are not usually regarded as of import in the elderly patient but, in



Fig XII 8 Bilateral subdural hematomas in an 83 year old man who died with tentorial herniation and mid brain crush

two cases of our 1954 series ruptured saccular aneurysms were the cause of death (fig XII 10) Both were on the anterior communicating artery One patient was 82 the other 85 In one there was only minimal atherosclerosis of the cerebral vessels and there was no hypertension In the other the atheromatous change was intense and hypertension was present We are of the opinion that hypertension may play some contributory part in the

fact of rupture and in the intensity of the bleeding. The influence of atheroma upon the fact of rupture is less clear cut. Although Walker and Allegre (21) have made an interesting case for the role of atheroma in the formation of saccular aneurysms, their well known association with extra cranial malformations and even other intracranial vascular malformations (22) would seem to point to an essentially anomalous character.

In contrast to the seccular aneurysms, fusiform arteriosclerotic aneurysms



Fig XII.9 A large left frontal parasagittal meningioma in a 76 year-old woman



Fig XII 10 Ruptured saccular aneurysm with meningo cerebral hemorrhage in an 81 year old hypertensive woman who survived 7 days after her collapse

require a combination of hypertension and atherosclerosis These lesions occur with greatest frequency in the vertebral basilar system and Denny Brown and I (23) have discussed some of their manifestations In this location they are seen as elongated tortuous dilated vertebral and basilar arteries (fig XII 11) The dilatation is likely to be segmental with points of stenosis dividing the segments The tortuosity may be so extreme that the vertebral arteries run obliquely across the medulla forming in the lower part of the lateral recess to join the basilar artery which then runs obliquely across the pons to the upper part of the opposite lateral recess The ostia of the smaller branches may be obliterated and the walls of these smaller branches may be greatly thickened (fig XII 12)

The sequence of development of these arteriosclerotic fusiform aneurysms begins with severe atheromatous degeneration of the vessel wall The internal elastic membrane and the muscular coat are disrupted and replaced (fig XII 13) Increased intraluminal pressure then results in constant distention of the inelastic vessel wall and small hemorrhages and dissections appear The atheromata break down in an irregular distribution at first so that bulbous protrusions appear and eventually the whole segment becomes thin walled and dilated Physiologically then, the vessel

becomes only an inelastic and non muscular hollow tube through which blood must be pushed against gravity The area of supply of such a vessel is readily compromised and episodes of insufficiency are almost the rule In addition the wide course the aneurysms must take into the lateral recess of the posterior fossa allows them to produce pressure effects on the cranial nerves so that facial spasm, deafness vertigo and facial pain may be the result Rupture with subarachnoid hemorrhage can occur In one of



Fig XIII.11 A typical fusiform atherosclerotic aneurysm in a 75 year old hypertensive diabetic woman The carotid arteries were similarly dilated and tortuous and death resulted from rupture of the left carotid artery

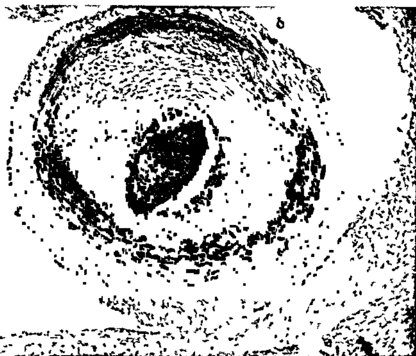


Fig XII 12 Thickened wall and narrowed lumen of the posterior inferior cerebellar artery of a 68 year old hypertensive woman with atherosclerotic aneurysmal deformities of the vertebral basilar system



Fig XII 13 Section from the wall of an atherosclerotic aneurysm of the basilar artery There is loss of the internal elastic lamina compression and thinning of the media and the atheromata are disintegrating

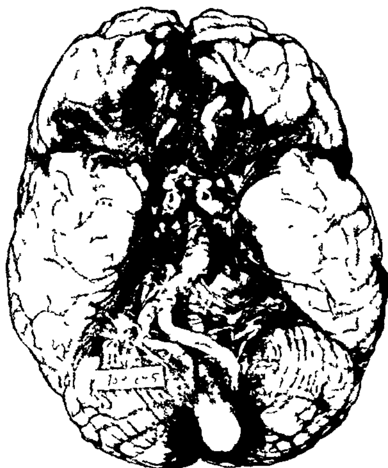


Fig XII 14 Massive subarachnoid hemorrhage in a 64 year old hypertensive woman The vertebral arteries are very tortuous There is marked stenosis at the junction of lower and middle thirds of the basilar artery The basilar above this point was very thinned in all parts A 3 mm rupture was present on the pontine surface of the mid portion of the basilar artery

our cases an arteriosclerotic aneurysm of the carotid artery ruptured into the cavernous sinus producing an arteriovenous fistula In another instance in a 61 year-old man there was a fatal rupture of the mid portion of the basilar artery (fig XII 14)

THERAPY OF CEREBROVASCULAR DISEASE IN THE ELDERLY

In recent years there has been increasing interest in the therapy of hypertension and even of arteriosclerosis New surgical procedures and power

ful pharmaceuticals have been employed to reduce blood pressure In the enthusiasm of the early use of such methods all kinds of patients were subjected to the miracle of an allegedly normal blood pressure until soon the warnings began to appear, that rapid reduction of blood pressure in the elderly beneficient as the effect may be on heart size and renal function can produce damage to the brain It has now been generally agreed that rapid reduction of blood pressure in the elderly at least is indicated only when there is hypertensive encephalopathy As we have mentioned earlier this is a relatively rare situation in the elderly, and so strong hypotensive agents have only a rare justification in this group In terms of therapy there is a corollary to these studies that the elderly patient must be protected against the accidental or deliberate drops in blood pressure associated with his disease or with treatments for his disease It should be kept in mind that a blood pressure drop is not a usual accompaniment of cerebral infarction *per se* When an elderly patient with a stroke presents with a low blood pressure immediate steps must be taken to restore blood pressure and to find the extracerebral catastrophe which precipitated the stroke

Failing in the first place to see the rationale of stellate ganglion block, we become discouraged in our early efforts with it and have abandoned its use entirely in the management of cerebral infarct

A therapeutic approach of more recent interest is the use of anticoagulants as prophylaxis against cerebral infarction Earlier studies by the New York Hospital group (24) were concerned with the use of anticoagulants and some encouraging results were reported in the prevention of cerebral embolic infarction More recently the Mayo Clinic group (25) has been concerned with the use of anticoagulants in impending infarction due to cerebrovascular insufficiency especially in the vertebral basilar system In cases of basilar insufficiency they regard anticoagulants as an emergency measure The efficacy of such a method of treatment has not yet been proved and it must still be regarded as experimental The mechanism of so-called anti-coagulant therapy in the prevention of non-embolic infarction is obscure The clinical as well as the pathologic data make it difficult to understand how the prevention of intra vascular clotting can be effective A patient develops the sudden onset of symptoms and signs relating to the brain stem and then clears rapidly within a few minutes returning to normalcy A few hours later the episode is repeated and again recovery occurs And so for several episodes over hours or days or weeks the sequence of loss of function followed by return to normal occurs until at last an episode no different from the others takes place except that now there is no recovery Did all of the earlier episodes with recovery mean that intravascular clotting had occurred? Was a new clot formed each time an

episode occurred—and if so what happened to the previous one? Examination of the vessel involved shows as often as not that there is no intravascular clotting that the basic pathologic process is an old chronic atherosclerotic stenosis or obliteration of the vessel Yet this is the kind of clinical problem in which anticoagulant therapy may delay or prevent the final catastrophe of infarction

The other possible explanation for a favorable action of anticoagulants on the episodic loss of function in cerebrovascular disease may lie in the physical effects of these substances upon the column of blood beyond the

[illegible] they do prevent the sludged blood from adhering to the walls of smaller blood vessels (?6) These properties suggest the possibility that the anti-coagulants are effective by reducing the cerebrovascular resistance thus allowing for greater cooperation from the fixed collaterals when an area of brain is compromised in a hemodynamic crisis We know of no measurements of cerebral blood flow cerebral oxygen uptake or cerebral vascular resistance in patients who are on effective doses of anticoagulant therapy

Our own experience with anticoagulants in the management of cerebrovascular disease has been restricted to those patients in whom there are transient recurrent losses of function without final clinically obvious infarction We are guardedly optimistic about the results in this group We have been reluctant to employ anticoagulants when infarction is established and especially when there is embolic infarction Further clinicopathologic studies may prove such reluctance to be poorly advised

Even if anticoagulants prove of value in a large and well controlled ser[illegible]

[illegible]

physical exertion are a few of th[illegible]
an excessive strain upon the com[illegible]
of the elderly patient are in the [illegible] category of cerebro-cardiovascular insufficiency and correlate well with advanced cerebral arteriosclerosis although not always with dementia or cerebral infarction There
can often be [illegible]
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in the frequency and [illegible]

Rusek Russek

therapy of cerebral infarction, with a view to reducing the cerebral edema and inflammation of the lesion They report that no significant untoward effects from cortisone were noted, although their 35 cases included 21 hypertensives and six diabetics This method of treatment of the acute cerebral infarct is still in the experimental stage, and has obvious elements of danger Acute infarction in the total or near total distribution of a major cerebral artery is always associated with a massive increase in intracranial pressure If cortisone proves capable of modifying the early inflammatory response to infarction, it may prevent the foraminal, tentorial and subfalcial herniations which compound the damage to the brain and are so often the cause of death

SUMMARY AND CONCLUSIONS

The material presented reinforces the generally accepted opinion that degenerative cerebral vascular disease is a formidable cause of disability in the elderly From a large autopsy material it is evident, however, that many people can attain very advanced years without suffering any significant cerebral effects from degenerative vascular disease

The diagnosis of cerebral vascular disease in the elderly must be made on positive grounds, and many tragedies of misdiagnosis may occur when it is assumed that a cerebral disorder must be vascular because the patient is elderly 'Little strokes' should be diagnosed only when there is reasonable evidence that a lacunar infarct has occurred

Emphasis is laid upon the extracranial factors, particularly cardiac, which underlie cerebral infarction The cerebral infarct of the elderly is viewed as one event in a diffuse circulatory disorder The therapeutic implications of such an approach are discussed

DISCUSSION

RAYMOND D ADAMS [Boston Mass] I believe that you will agree that the subject which Dr Foley has reviewed is one of the most important in all of medicine and it deserves our closest attention Vascular disease of the brain not only in the senescent but in the middle aged as well ranks first in frequency and gravity amongst all diseases of the brain leading as a rule to a state of serious disability and even death

What are the significant recent developments in this field of medicine which promise some hope of a more complete understanding of apoplexy? Firstly I should say that studies during the last two or three decades have shown that arteriosclerosis is not one disease but several It includes such conditions as Monckeberg's calcific medial sclerosis atherosclerosis hyperplastic arteriolosclerosis hyaline arteriosclerosis necrotizing arteriolar disease capillary fibrosis and in the brain a peculiar deposition of pseudo calc Each of these diseases has a morphology and a distribution within the vascular system all its own Atherosclerosis and embolism are major causes of blockage of large arteries and a recognizable clinical event in the form of a stroke is the usual result Hemorrhage is still of uncertain cause but is no doubt closely related to high blood pressure Dr Foley's data which disclose a high frequency of vascular lesions in the brains of elderly

persons agrees closely with that from our laboratory where it was found that approximately 25 per cent of all patients dying in a general hospital had gross evidence of cerebrovascular disease If microscopic examination had been performed in each case the percentage of abnormal brains would have been higher The lesser incidence of brain hemorrhage in the senescent than in middle aged individuals is noteworthy and may be attributed to the fact that this form of brain disease prevents survival to the senium It does not accord well with the idea that atherosclerosis has an important role in the rupture of brain arteries

Secondly clinical and clinical pathologic studies have led to the definition of many different forms of vascular diseases and at the same time have informed us of ways by which we may identify these diseases during life Atherosclerotic thrombosis with brain infarction embolism with brain infarction recurrent ischemic cerebral attacks brain hemorrhage and ruptured saccular aneurism can now be dealt with at a purely clinical level The importance of this advance in clinical neurology can hardly be over estimated If diseases of such different cause and mechanism could not be distinguished any comparative study of methods of therapy would be quite futile Stroke shock or an apoplectic attack is the common denominator of all these diseases and without it diagnosis is always questionable The stroke may be major or minor and the latter may be overlooked However Dr Foley s caution in regard to the diagnosis of little strokes should be heeded lest too many cases with trivial symptoms be forced into the vascular category

Thirdly increasing attention has been given to some of the mechanisms of apoplexy and even occlusion of an artery and brain infarction can be shown to depend on the operation of many factors Dr Foley s example of arterial narrowing with a fall in systemic blood pressure leading to a lack of circulation in that vascular territory is pertinent However in my experience this latter set of circumstances rarely obtains in pure form and it probably represents an over simplification The mechanism of the recurrent ischemic cerebral attacks all of identical pattern remains in doubt [illegible]

[illegible] that atherosclerosis and hypertension are not invariable accompaniments of the aging process The importance of dietary factors heredity etc is being investigated systematically in many quarters [illegible]

[illegible] is reviewed [illegible]

[illegible] disease of the [illegible]

[illegible] appear to occur with increasing frequency in the aged and which could influence the nutrition of the nerve cells and other elements of the tissues These changes will probably require ultramicroscopic techniques for their investigation and I would like to ask Drs Lansing and Foley if they have performed or know of such studies having been made on the small vessels of the brain

DR H HOUSTON MERRITT [New York N Y] Dr Foley and Dr Adams have covered the subject so well that there is little to add There is one point that can be emphasized that is the vast majority of cerebrovascular lesions are the result of arteriosclerosis and arteriosclerosis is a disease and not a normal accompaniment of age

Dr Foley also emphasized that all old people who suffer discomfort at any time are not necessarily having little strokes These have been popularized so much that we are creating a national neurosis among our middle aged and elderly people

PRESIDENT MOORE Are there any other comments from members of the Commission? If not I have two questions for Dr Foley from the floor When there is gross sclerosis of the cerebral arteries in what percentage of the cases is there diminution of the lumen? There is evidence from cerebral angiography that in most cases of cerebral arteriosclerosis there is actually an increase rather than a decrease in the lumen of the vessel The second question is Is there any experience available on the effect of the widely advertised glutamic acid preparations in arteriosclerosis of the brain? Will Dr Foley close the discussion?

DR JOSEPH FOLEY I am very grateful to the discussors It is always easier to be grateful when people agree with you

I should like to answer first the question about whether in sclerosis of the cerebral arteries there is stenosis or dilatation by reminding you of Dr Adams first comment about the many kinds of arteriosclerosis Certainly in some kinds of hypertensive disease when there is co existing arteriosclerosis there is likely to be some dilatation of the cerebral vessels The fusiform aneurysms which I demonstrated are really full blown There are many preliminary degrees of this change of course

I myself am very dubious about the correlation of what one sees in the arteriogram with what one sees at the autopsy table except in the broadest sense Arteriography is a magnificent tool no doubt is still an indirect method of visualization and subject to all the hazards of indirect visualization

In regard to glutamic acid I can only say that I do not use it and have no experience whatsoever with it

Dr Adams emphasis upon hemorrhage and its relation to hypertension is of extreme importance There has been as you know experimental work suggesting that hemorrhage in the brain has other mechanisms besides hypertension Actually the only other conditions of any numerical significance are trauma malformation and blood dyscrasia

Dr Adams pointed out also the difficulties in documenting the factors that precipitate infarction I used hypotension deliberately because it is one of the few that we can document but we cannot document it with the frequency that we would like to There must be other methods that we can use to provide documentation and I would not want to leave you with the impression that hypotension is the only kind of diffuse circulatory derangement that precipitates the infarction Coronary insufficiency rather than infarction seems to precede many cerebral infarctions in our own material

Dr Adams has raised the question of the relation between senile atrophy and changes in small blood vessels This is to me an almost insoluble problem by present methods I don t know which is the cart and which is the horse It may be that pericapillary fibrosis is simply another manifestation of brain atrophy

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CHAPTER XIII

NEUROLOGICAL CHANGES IN THE AGED

MACDONALD CRITCHLEY

There is something artificial about restricting to the central nervous system a discussion of aging The only excuse is that in a symposium such as this it is convenient to parcellate the subject matter A neurologist is in a particularly strong position to contribute towards the total problem in that his specialty can be said to embrace the psychologic and psychiatric attitudes and to include a histologic study of the highly sensitive and fundamental organ of personality mentation and behavior—in other words the physical counterpart of the organism

Much of what a neurologist can contribute is purely factual and entails a mere descriptive approach He supplies the bricks and mortar which may eventually be incorporated within the edifice of our understanding of the nature of aging processes in general But description is not enough It is a relatively simple matter to make precise observations be they psychometric clinical histologic or clinical upon the complex problem of the neurology of old age To comprehend these findings however and to apply them are matters which are much more difficult to accomplish and yet at the same time they are far more valuable I shall therefore first merely record the simple facts about the senile nervous system Secondly I shall try to indicate in more speculative fashion where the data may perhaps assist our approach to an eventual threefold goal—namely an understanding of the nature of the processes of aging the securing of mental and physical efficiency throughout the senium and the extension of the life span

Unfortunately the aging of the nervous system cannot be regarded as a clean or tidy experiment on the part of nature The subject matter is much too overlaid with epiphenomena and coincidentals Among the many inherent difficulties of the research we can enumerate two in the first place side by side with the aging of the central nervous system properly speaking degenerative alterations are also taking place in the cerebrospinal vasculature These changes of themselves are likely to produce additional manifestations To separate the pathologic and clinical evidences of primary involution from those of focal or general anoxia is no easy matter

Secondly in the aging of the nervous system (quite apart from its vasculature) we are doubtless observing a dual phenomenon being partly physiologic and partly pathologic The former includes the pure uncompli

cated evidences of simple involution the final stages of a life long biologic process of development maturity and decline Such changes are natural inevitable and irreversible This side of the problem may be spoken of as constituting the primary aspect of aging The secondary or pathologic aspects comprise the *senium ex morbo* made up of the accumulated sequelae which remain like scars bearing witness to the strains stresses and wear and tear of a long life together with the ravages of ill health self indulgence disease injury and malnutrition which have been going on ever since birth This aspect of the problem is additional accidental—avoidable perhaps—and even reversible to some extent

These two classes of pathologic phenomena are sometimes also correlated with the origins of the aging processes and are thus spoken of as the primary and secondary *causes* of the aging of the nervous system Or they may be called endogenous as opposed to exogenous causes of decay In this way it seems possible to reconcile the adherents of two rival schools of thought who have hitherto not been able to agree as to the essential nature of senescence On the one hand there were those who held the view that aging is biologic and natural (1 2) The opponents regard old age as a disease in itself (3–6) A compromise must surely be struck between those extremists in either camp Let no one assert that this discussion is a mere scholastic quibble one which need not be taken seriously The fundamentals of gerontology turn upon a scrutiny of this important difference of opinion [1]

In so far as a study of the neurology of old age promises to illuminate our knowledge of aging processes we may assert that psychology and psychiatry probably offer rather better prospects for research than a simple semeiologic approach Thus the vexed question of relationship between the mental life of the normal senescent and that of the senile dement is one which still provokes discussion (10–15) But this important topic is the responsibility of other speakers My task however artificial in its restr-
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n ... ted to clinical matters and the interesting subject of the pathology of the aging nervous system will not be undertaken

[1] How to define the process of aging is a question wh...
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ample in the small muscles of the hand Should there be concomitant deformities in the joints of the wrists and fingers then an arthritic muscular atrophy is often demonstrable over and above the senile amyotrophy Fibrillation and fasciculation do not usually appear in cases of senile muscular atrophy except in certain morbid conditions which will be considered later

Tremor [illegible]

read " the keepers of the house (*i e* the hands) shall tremble

Although close and accurate testing of common sensibility is often a matter of extreme difficulty in the aged it is quite easy to determine that the threshold for light touch and more especially for pain is definitely raised Even better known is the fact that the appreciation of a vibrating tuning fork tends to lessen with advancing years (18–21) Blunting of vibratory sensibility is commonly ascribed to defective vascularity of the white matter of the spinal cord This hypothesis does not explain the factor of selectivity *i e* why the function of certain long tracts such as the lateral columns should be unaffected while some of the ascending pathways are involved While upon this topic we recall the pathologic changes found by Fluegel (22) in the spinal cord of a series of six persons over 80 years of age despite une intégrité fonctionelle presque complète Unfortunately the author did not specify the precise neurologic findings on his patients

Within the domain of the special senses a similar dulling of the acuity of perception may be found leading to presbyopia presbyacusis and presbyageusia These objective findings within the afferent nervous system tally with the ordinary clinical experience that in the aged many general diseases, and also injuries seem to be attended by less pain than might be expected

Many of the reflex phenomena used in routine testing behave differently in the case of the aged subject Thus the tendon jerks may prove difficult to elicit This is particularly so in the case of the ankle jerks which are not infrequently quite unobtainable The knee jerks usually persist however Arm reflexes (supinator biceps and triceps jerks) occupy a position midway between the behavior of the knee and ankle jerks

Loss of ankle jerks in old people may be the consequence of inelasticity of the tendo achilles rather than necessarily of changes within the reflex arc at a spinal level

Increasing difficulty in the elicitation of the abdominal responses is well known they may indeed be unobtainable as early in life as middle age This is so largely because of the frequency with which the musculature has been overstretched either by childbearing or by adiposity

The neurologic changes in the aged will be discussed under two headings. First of all the neurologic signs of "normal" aged individuals will be described. Secondly, certain neurologic disorders will be dealt with, which are often regarded as being specifically senile in character.

THE NEUROLOGIC SIGNS OF "NORMAL" AGED PERSONS

Every experienced clinical neurologist realizes that the ordinary standards of diagnosis do not apply to the very aged—that is, those lingering on into the tenth and eleventh decades of life. In other words, the hallmarks of the "normal" nervous system are not necessarily valid within the senium.

Unless we constantly bear in mind the fact that our standards of normalcy are different in the aged than in adulthood, we run the risk of diagnosing neurologic disorders where none actually exists. It needs to be stressed, therefore, that with advancing years certain changes occur so often as to be discounted as evidence of disease (16, 17). Chief among the deviations are the following.

Pupillary changes. These comprise a tendency towards miosis together with a sluggishness in reflex response to light and also on accommodation. A stage may be reached and later surmounted when the pupils are inactive to light though still contracting on accommodation. These clinical changes are the result of alterations within the musculature of the sphincter pupillae including fibrosis, hyalinization and lipoid infiltration.

Ocular movements. With advancing years there is a progressive restriction in the movement of convergence. Defective conjugate upward gaze is also a common "normal" finding in the elderly.

Special mention may be made here of the familiar ocular evidence of aging—namely the presence of an arcus senilis or gerontoxon. This represents merely the most conspicuous manifestation of a much more widely spread lipoid infiltration of the tissues including the iris, ciliary body, the sclera, and the membranes of Bowman, Descemet and of Bruch. The earliest sign is a crescentic strip of cloudiness in the lower sector of the cornea; later a similar arc appears in the upper part ordinarily covered by the eyelid. Later still these arcs fuse to form a ring-like structure separated from the rim of the cornea by the narrow "lucid interval" of Vogt. The relationship of the arcus senilis to chronologic age is not straightforward, nor indeed is the correlation with arterial degeneration very close. There may perhaps be a closer correlation between arcus senilis and hypercholesterinemia, for a similar condition has been produced experimentally in rabbits by overfeeding with cholestrol. Further clinical studies of the incidence of the arcus senilis are needed with special reference to its distribution within the aged population.

Muscular wasting is commonly found in advanced old age as a thinly spread generalized amyotrophy. The histologic counterpart is a shrinkage both in the number of muscle fibers and in their individual bulk. Often this muscular wasting is particularly conspicuous in certain regions—for ex

An attitude of general flexion is also one of the hall marks of old age Head and neck are held craned forward there is a gentle dorsal kyphosis upper limbs are bent at elbows and wrists while the hips and knees are also slightly flexed Here again we may quote the twelfth chapter of Ecclesiastes where we find the strong men (i e the legs) shall bow themselves In marked cases the degree of flexion may be extreme and mimic advanced Parkinson s disease When the old person lies supine his neck may remain bent so that the occiput is off the pillow Abnormal attitudes of the hands are very common and indeed the appearance of the hands is only too often a revealing indication of the age of the individual Here as elsewhere joint deformities may exaggerate the involutional picture

We are probably justified in attributing the flexed attitude of old age in part at least to extra pyramidal factors But we must certainly not overlook the role played by other associated changes in the vertebral column and in the intervertebral discs ankylosing disorders of the ligaments and joints shrinkage and sclerosis of the tendons and muscles which all contribute to the total picture Indeed we must not forget that some extreme cases of arthritis deformans and of spondylose rhizomélique superficially resemble a parkinsonian syndrome and may sometimes occasion diagnostic confusion Muscular rigidity is another common finding in the aged especially when considerable cerebro-vascular degeneration is also present Foerster spoke of this cond tion as an arteriosclerotic rigidity It is demonstrable clinically by a uniform resistance to passive manipulations especially in the limbs and in the neck Proximal segments of an extremity are more affected than the distal legs more than arms At the bedside it becomes obvious that the phenomenon of rigidity is no simple matter There is even a mental component in many cases especially when arteriopathy coexists Thus the rigidity may vary directly with the amount of force used by the examiner in passive manipulation Again if the patient s attention is distracted from the maneuvering of the limbs the rigidity becomes less Th s fact often leads to the assumption that the s h

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Mental influences which affect the motility of the aged may also be traced in a tendency towards motor perseveration—itself an expression of ideational inertia To some extent senile or arteriosclerotic rigidity may be

The plantar responses are often very difficult to interpret in the aged While a frank extensor response must be regarded as an exceptional finding it is equally true that a clear-cut flexor response is but rarely seen Various factors combine to complicate the test Deformities of the feet with valgus or equinovalgus resting attitudes of the great toe stiffness or ankylosis of the first metatarso phalangeal joint hardening of the skin of the sole with relative insensitivity—these are some of the common conditions which make it difficult for the clinician to elicit a response or to interpret whatever movement should occur

*It would be unwise to conclude that the foregoing reflex phenomena nec*essarily indicate an underlying structural senile alteration within the nervous system Involutional changes in the muscles tendons ligaments and peri articular tissues probably play an important part in making these superficial and tendon reflexes sluggish or unobtainable

In contemplating the clinical effects of aging of the nervous system we arrive at some interesting and perhaps unexpected ideas The involutional process is a diffuse one affecting all levels of the neuraxis simultaneously It is tempting to regard the resulting picture as a clinical expression of a gradual dissolution of the nervous system in the Jacksonian sense Such a dissolution might be expected more or less to recapitulate in reverse some of the evolutionary stages Older mechanisms should prove more resistant to change younger structures and functions being more vulnerable

Clinical experience does not altogether bear out this anticipation A neurologist studying the aging of the nervous system from a structural standpoint—leaving aside purely mental functions—might well comment upon the relative infrequency of signs of cerebellar defect and also of pyramidal impairment But on the other hand certain extrapyramidal manifestations are very common If one can make a distinction here between hyperkinetic and akinetic extrapyramidal signs we can emphasize that it is the latter type of change which we witness in old age Tremor apart such spontaneous movements as dystonia athetosis chorea are rare indeed they hold no place within the neurologic picture of normal old age

Common in the aged however are the so-called akinetic hypertonic signs which in their fullest development constitute a parkinsonian like amyostatic syndrome without tremor (16 23) Minor extrapyramidal *signs are so commonly present in the aged that they are apt to be over*looked or rather to be put down to a general loss of the elasticity of the tissues But most of those numerous little signs and manifestations the characteristic gestures the attitude stance and gait of the elderly—distinguishing them so sharply from the youthful are really features of an extrapyramidal order Thus the young actor in assuming the role of an old man actually adopts and unwittingly assumes many components of an extrapyramidal syndrome

An attitude of general flexion is also one of the hall marks of old age Head and neck are held craned forward there is a gentle dorsal kyphosis upper limbs are bent at elbows and wrists while the hips and knees are also slightly flexed Here again we may quote the twelfth chapter of Ecclesiastes where we find the strong men (*i e* the legs) shall bow themselves In marked cases the degree of flexion may be extreme and mimic advanced Parkinson s disease When the old person lies supine his neck may remain bent so that the occiput is off the pillow Abnormal attitudes of the hands are very common and indeed the appearance of the hands is only too often a revealing indication of the age of the individual Here as elsewhere joint deformities may exaggerate the involutional picture

We are probably justified in attributing the flexed attitude of old age, in part at least, to extra pyramidal factors But we must certainly not overlook the role played by other associated changes in the vertebral column and in the intervertebral discs ankylosing disorders of the ligaments and joints shrinkage and sclerosis of the tendons and muscles which all contribute to the total picture Indeed we must not forget that some extreme cases of arthritis deformans and of spondylose rhizomélique superficially resemble a parkinsonian syndrome and may sometimes occasion diagnostic confusion Muscular rigidity is another common finding in the aged especially when considerable cerebro vascular degeneration is also present Foerster spoke of this condition as an arteriosclerotic rigidity It is demonstrable clinically by a uniform resistance to passive manipulations especially in the limbs and in the neck Proximal segments of an extremity are more affected than the distal legs more than arms At the bedside it becomes obvious that the phenomenon of rigidity is no simple matter There is even a *mental* component in many cases especially when arteriopathy coexists Thus the rigidity may vary directly with the amount of force used by the examiner in passive manipulation Again if the patient s attention is distracted from the maneuvering of the limbs the rigidity becomes less This fact often leads to the assumption that the subject is "not relaxing But it would be wrong to dismiss this finding as a mere accidental complicating factor—the evidence of wilful *non*-cooperation on the [illegible] aged patient [illegible] of the examine[illegible] luce an auton[illegible] tightening of the [illegible] opposit[illegible] negati[illegible] non o[illegible] brou[illegible] M[illegible] in a [illegible] —itself an expression of ideation in inertia To some extent senile or arteriosclerotic rigidity may be

The plantar responses are often very difficult to interpret in the aged. While a frank extensor response must be regarded as an exceptional finding, it is equally true that a clear-cut flexor response is but rarely seen. Various factors combine to complicate the test. Deformities of the feet with valgus or equinovalgus resting attitudes of the great toe, stiffness or ankylosis of the first metatarso-phalangeal joint, hardening of the skin of the sole with relative insensitivity—these are some of the common conditions which make it difficult for the clinician to elicit a response or to interpret whatever movement should occur.

It would be unwise to conclude that the foregoing reflex phenomena necessarily indicate an underlying structural senile alteration within the nervous system. Involutional changes in the muscles, tendons, ligaments and periarticular tissues probably play an important part in making these superficial and tendon reflexes sluggish or unobtainable.

In contemplating the clinical effects of aging of the nervous system, we arrive at some interesting and perhaps unexpected ideas. The involutional process is a diffuse one, affecting all levels of the neuraxis simultaneously. It is tempting to regard the resulting picture as a clinical expression of a gradual dissolution of the nervous system in the Jacksonian sense. Such a dissolution might be expected more or less to recapitulate in reverse some of the evolutionary stages. Older mechanisms should prove more resistant to change, younger structures and functions being more vulnerable.

Clinical experience does not altogether bear out this anticipation. A neurologist studying the aging of the nervous system from a structural standpoint—leaving aside purely mental functions—might well comment upon the relative infrequency of signs of cerebellar defect and also of pyramidal impairment. But on the other hand certain extrapyramidal manifestations are very common. If one can make a distinction here between hyperkinetic and akinetic extrapyramidal signs, we can emphasize that it is the latter type of change which we witness in old age. Tremor apart, such spontaneous movements as dystonia, athetosis, chorea are rare indeed; they hold no place within the neurologic picture of normal old age.

Common in the aged, however, are the so-called akinetic hypertonic signs, which in their fullest development constitute a parkinsonian-like "amyostatic" syndrome without tremor (16, 23). Minor extrapyramidal signs are so commonly present in the aged that they are apt to be overlooked or rather to be put down to a general loss of the elasticity of the tissues. But most of those numerous little signs and manifestations, the characteristic gestures, the attitude, stance and gait of the elderly—distinguishing them so sharply from the youthful—are really features of an extrapyramidal order. Thus the young actor in assuming the role of an old man actually adopts and unwittingly assumes many components of an extrapyramidal syndrome.

At the same time it must be emphasised that the so-called 'associated movements' (which may be said to include all secondary movements, synergias and movements of co-operation) are not actually in abeyance but are merely reduced in amplitude and speed

Finally the extrapyramidal like picture is completed by a characteristic slowness of movement We may not perhaps altogether understand what it is that determines the rate of a particular movement—willed voluntary, volitional automatic instinctive—in a normal young adult Unquestionably however this rate is reduced in the aged just as it is in victims of Parkinson's disease Slowness also involves actions which can be roughly termed automatic rather than highly volitional Thus the passage of the fork to the mouth at meal times the champing of the jaws the flicking away of a fly from settling upon the brow—all these actions are just as retarded as those which are deliberately executed in response to a command

The foregoing components of extrapyramidal impairment—namely a flexion attitude rigidity infrequency and slowness of movement—constitute when intense a sort of parkinsonian state But in minor degree they are so commonly met with in normal old people as to establish a hall mark of the aging nervous system It might therefore be argued that the extrapyramidal system though commonly regarded as the old motor system is apparently more vulnerable to aging processes than some of the younger corticifugal efferent pathways Or perhaps the matter could be better expressed in somewhat different terms Can it be that the clinical expression of a diffuse thinly spread neuropathologic process is to be seen in an extrapyramidal picture rather than say a pyramidal or hyperkinetic, or cerebellar or sensory syndrome? Extrapyramidal signs in other words may comprise a sort of clinical least common multiple of neuronic dissolution

NEUROLOGIC DISORDERS PECULIAR TO THE SENIUM

The recognition of neurologic disease in the aged is compl[illegible]

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[illegible] is not strictly relevant A third complicating factor is more difficult The nervous system of a very old person may be involved secondarily—that is to say as the result of primary senile disease of extraneural tissues For example neurologic syndromes may complicate a spondylosis or disc degeneration Still more difficult to extricate are the neurologic disorders which are consequent upon primary

looked upon as an index of perseveration whereby rapidly alternating passive movements tend to be resisted This mental influence is shown by two phenomena In the first place after a limb has been passively flexed and extended several times and then abruptly released the patient may continue to make feeble flexion-extension movements thus actively simulating the passive movements carried out by the examiner These palipraxic after movements continue for only a short time The second illustration of a mental influence consists in the assumption of catatonic postures The aged person may allow his limb to be retained in whatever position it is placed even in defiance of gravity Such a phenomenon results from a combination of extra pyramidal factors with some degree of dementia This is probably what Steck had in mind when he spoke of catatonia as being a link connecting organic with functional phenomena (25)

As I have written elsewhere (23) defective mentation is an important influence *in determining catatonia in cases of senile (or arteriosclerotic)* rigidity Inadequate perception lack of attention and retarded cerebration combine to produce an ideational inertia or mental viscosity The subject fails to grasp successive concepts if they should follow too close one after another If the suggestion takes the form of an attitude passively imposed upon a limb the posture tends to be maintained for an inordinate length of time Two explanations are possible Either the subject is temporarily oblivious of the existence of the limb the proprioceptive impulses failing to attain awareness or on the other hand the subject s sensorium may be replete with the idea of the attitude which has been passively ordained to the exclusion of fresh ideas Not until the initial suggestion wanes or is replaced by awareness of the painful impulses from the tiring muscles is the catatonic attitude interrupted

Another motor sign characteristic of extrapyramidal disorder is to be found in a general poverty of movement Although the aged person is not paralysed in any sense of the word he seems to make as few movements as possible He does not exert himself but behaves as though the effort to move were too great This relative immobility shows itself in the impassive facial expression the infrequent blinking of the eyelids and the statuesque attitude so typical of those advanced in years When he wishes to look far over to one side or the other the elderly person moves his eyes first Then the head neck and shoulders slowly follow and all in a piece The quick nervous gestures the bird like movements of so many vivacious young persons the movements of rhetoric expression and emotional display are not seen in the aged In their stead a certain poise or calmness is found Old people sit for long periods without changing their position crossing and uncrossing their legs folding their arms fidgeting with their hands or gazing around

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disease of the cerebrospinal arterial system. Lastly, there remain the senile disorders of the nervous system which can be regarded as "pure" or specific. In ordinary practice the two last groups of case occur so intimately linked that to disentangle them becomes a rather artificial task.

It is interesting to recall the records of 16,000 patients compiled by Lewellys Barker (26). Out of this series there were 300 patients who applied for consultation over a period of seven years. Of this total, 210 cases were in the seventh decade of life, 57 were in the eighth, and 3 were in the ninth. The subjective complaints of the 210 patients aged between 60 and 70 years were analyzed, and it was found that by far the commonest symptoms were referable to the nervous system. These comprised 1) depression (23 cases) 2) nervousness (26 cases) 3) fatigability (23 cases) 4) insomnia (20 cases) 5) anxiety (13 cases) 6) acroparesthesias (11 cases) 7) headaches and other cephalic sensations (10 cases) 8) dizziness (9 cases) 9) visual disturbances (9 cases) 10) tremor (8 cases) 11) failing memory (5 cases) 12) fainting spells (5 cases) 13) deafness (5 cases) 14) disorders of speech (3 cases) 15) tinnitus (3 cases) 16) difficulty in walking (2 cases) and 17) sciatica (2 cases). When the final diagnoses were analyzed it was found that nervous maladies took second place to circulatory affections. The neurologic diagnoses included psychogenic disorder (13 instances), Parkinson's disease (7 instances), senile psychosis (4 cases), paralysis secondary to organic brain disease (3 cases), and organic encephalopathy of doubtful nature (3 cases).

Lewellys Barker's figures may be compared with one's own case records taken from a consulting neurologic (and non-psychiatric) practice. In the nine-year period 1946–1955, 252 new patients of 70 years of age and over were seen in private practice. (Hospital patients are not included.) The diagnoses arrived at in these cases may be set out in tabular form (Table I).

The genuine specific neurologic disorders of the senium are few in number and rare in occurrence. Certain clinical syndromes deserve attention, particularly senile tremor, senile paraplegia, the senile muscular atrophies, senile epilepsy, and giant-cell arteritis.

Senile tremor. Tremor has been regarded for centuries as a normal and integral appanage of senility. It is strange that this idea has persisted despite the evidence afforded by neurologists that tremor in old age is actually an uncommon feature. As long ago as 1876 Charcot (27) registered a protest, and he estimated that out of an aged population of about two thousand inmates of the Hospice de la Salpêtrière, instances of tremor numbered no more than thirty.

Nowadays it is realized that senile tremor is merely a particular example of essential or *idiopathic tremor happening to appear first in extreme* age (28). Although this was the teaching laid down by Trousseau in 188

TABLE VIII 1

Diagnosis in 252 new patients over 70 years of age, 1946–1955

Diagnosis		Number of Cases
Cerebrovascular degeneration including hypertension, senile epilepsy, temporal arteritis, and peripheral vascular disease		107
Neurotic and psychotic problems including dementia depression, hypochondria con lusional states and anxiety (all exclusive of arteriopathy)		29
Parkinson's disease (excluding arteriosclerotic Parkinsonism)		23
Neuralgia		
trigeminal	10	
post herpetic	15	
other types	4	29
Headaches (? cause)		11
Backache		4
Spondylosis and spondylitis		6
Carcinomatosis with neurologic involvement		5
Cerebellar atrophy		5
Progressive spastic bulbar palsy (excluding "pseudo bulbar palsy")		3
Combined degeneration of the spinal cord		3
Senile paraplegia '		8
Acroparesthesia including the carpal tunnel syndrome		2
Sequelae of head injury including subdural haematoma		7
Peripheral neuropathy		
Diabetic	1	
Carcinomatous (included above)	1	
"Sciatica	3	4
Cerebral tumor (excluding metastatic carcinoma of the brain)		3
Senile (essential) tremor		1
Vertigo		1
Narcolepsy		1
Total		252

(29) it did not gain acceptance until quite recently That essential tremor is also familial tremor is yet another conception which developed slowly, even though it had been affirmed by Most in 1836 (30) When adequate pedigrees are available for scrutiny it becomes obvious that 'anticipation' is an important genetic property of these cases of tremor Thus, charac teristically senile tremor in the first affected generation crops up earlier and earlier in successive generations, and appears as a pre senile, an adult, a juvenile, an infantile, and finally a congen . .

Though the morbid anatomy of sen clinical features are familiar The t . head, jaw, or hands, or any combination of these regions In the head there may be a fine, nodding tremor (tremblement affirmatif'), or a side to side move

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It is interesting to recall the records of 16,000 patients compiled by Lewellys Barker (26). Out of this series, there were 300 patients who applied for consultation over a period of seven years. Of this total, 240 cases were in the seventh decade of life, 57 were in the eighth, and 3 were in the ninth. The subjective complaints of the 240 patients aged between 60 and 70 years were analyzed, and it was found that by far the commonest symptoms were referable to the nervous system. These comprised 1) depression (29 cases), 2) nervousness (26 cases), 3) fatigability (25 cases), 4) insomnia (20 cases), 5) anxiety (18 cases), 6) acroparesthesias (11 cases), 7) headaches and other cephalic sensations (10 cases), 8) dizziness (9 cases), 9) visual disturbances (9 cases), 10) tremor (8 cases), 11) failing memory (5 cases), 12) fainting spells (5 cases), 13) deafness (5 cases), 14) disorders of speech (3 cases), 15) tinnitus (3 cases), 16) difficulty in walking (2 cases), and 17) "sciatica" (2 cases). When the final diagnoses were analyzed it was found that nervous maladies took second place to circulatory affections. The neurologic diagnoses included psychogenic disorder (48 instances), Parkinson's disease (7 instances), senile psychosis (4 cases), paralysis secondary to organic brain disease (3 cases), and "organic encephalopathy of doubtful nature" (3 cases).

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ment (tremblement negatif) Tremor of the mandible shows itself as a persistent champing or chewing Sometimes there is a repetitive movement of the lower part of the face especially of the lips and of the mentalis muscle (cf Démange s patient (31) dubbed old rabbit face 1882) In the hands the tremor may be slow and coarse (1 per second) or finer and more rapid (12 per second) The former type is reminiscent of the parkinsonian tremor, while the latter resembles the tremulousness of hyperthyroidal states The tremor may be temporarily inhibited by willed movements of the limbs Or it may become exaggerated In the latter case the resemblances to a cerebellar type of tremor are very close Senile tremor is increased by fatigue by cold and by emotional stress Often it is temporarily relieved by taking alcohol Senile tremor may interfere with the performance of delicate finger movements and it characteristically distorts the hand writing Progressive attenuation of the script does not occur however and hence there is no real resemblance to the micrographia of the parkinsonian

Essential tremor is ordinarily not associated with rigidity poverty or slowness of movements and these are important criteria in excluding Parkinson s disease But in extreme old age some degree of rigidity hypokinesis and bradykinesis may happen to occur as part of the simple picture of old age Consequently it is more difficult to differentiate paralysis agitans from senile tremor than from essential tremor in a younger subject

No discussion of senile (essential) tremor can omit reference to the interesting assertion that Minor (32–36) Katzenstein (37) and others have made concerning the families of affected members Many authors have drawn attention to the presence of longevity and fecundity in the family trees a phenomenon which Minor termed the *status macrobioticus multiparus* Others have elaborated this idea and have claimed that patients with senile (essential) tremor are highly intelligent virile personalities who work hard and play hard eat heavily drink deeply and are sexually lusty Quite aside from this notion of macrobiosis there is evidence that in some families senile (essential) tremor constitutes a *forme fruste* of some other and better defined neurologic disorder Two diseases have been specifically mentioned in this connection pre senile cerebellar atrophy and Parkinson s disease As regards the latter we recall that no sharp nosological demarcation was believed to exist between Parkinson s disease and senile tremor by such authorities as Gowers (38) Pelnar (39) Gelma (10) and Noica (41) An association between senile tremor and senile cerebellar atrophy has been mooted by Schuster (12) and by Critchley and Greenfield (43)

Senile disorders of gait This term is deliberately chosen in preference to senile paraplegia for neither pathogenesis nor morbid anatomy is uni

form Paraplegia is also a misnomer at times for the clinical disability is more in the nature of a dysbasia or a mere difficulty in walking and actual paralysis as tested upon a supine patient—may not be demonstrable More satisfactory terms therefore would be senile disorders of gait or dysbasia occurring in old age (44)

Earlier neurologists wrote as though there existed a clear cut clinical entity characterised by paralysis of the lower limbs in old people and it is to Gowers (45) that we probably owe the term senile paraplegia It was first used in print by Kelly (46) Later experience has shown that the problem is far more complicated that weakness of the legs in old people can result from lesions at various levels in the nervous system and furthermore that even non neurologic alterations can produce difficulty in standing and walking The monograph of Lhermitte (47) enumerated the causes of paraplegia in the aged as cerebral spinal and muscular Nowadays it is usual to include various sub-cortical pathologies among the causes of disordered gait in the senium

Cortical paraplegia may occasionally occur in the aged as the result of an abrupt and solitary vascular accident This comes about when the anterior cerebral artery of one side happens to supply both cerebral hemispheres by way of an unusually large anterior communicating artery This anatomic anomaly is by no means rare In such cases an occlusion of the main trunk of the hypertrophied anterior cerebral artery will prod...

...c coral artery

In geriatric experience it is again not rare to find a bilateral weakness developing *after an isolated* apoplectic hemiplegia An aged person sustains a stroke which produces a one sided paralysis He takes to his bed As weeks go by and in the absence of nursing and remedial care the opposite non paralyzed leg becomes more and more stiff contra...

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... internally rotated Both knees are firmly pressed *together* and passive correction of the deformities is impossible

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... patient's motor power is tested as he lies in bed no great disability can be found But the patient cannot walk unsupported He may be most unwilling to make any attempt to do so Encouraged however he hesitatingly and fearfully advances in short shuffling steps frantically clutching the furniture or the bystanders After

a step or two the legs may give way the patient may stagger wildly or one leg may cross in front of the other This is the astasie trépidante of the French neurologists A variant is sometimes spoken of as Petrén s gait (48) Here the patient makes a few tiny steps and then comes to a standstill with coaxing however he steps out almost normally Again after a few paces he halts and is reluctant to proceed With further encouragement he starts again So it continues a few steps and then a pause and so on again

There has been some discussion as to the nature of this type of gait disorder (49) Some have looked upon the trouble as evidence of a senile hysteria *Others have regarded the disability as being apraxic in nature* (50 51) Quesnel (52) discussed functional disorders of gait as occurring in the aged and recognized three clinical groups 1) a mild and readily curable disability 2) more severe impairment associated with mental disease and 3) an organo functional type in which structural disease of the bones joints or nerves may be present In this third group belong those cases of functional paraplegia supervening in patients bed ridden because of a fracture

It is also common to see in aged subjects the characteristic difficulties in walking which are so typical of the arteriopath Here belong the small steppage gait of the patient with progressive lacunar disintegration with pseudo bulbar palsy or with arteriosclerotic parkinsonism Sometimes the gait is so disordered as to be ridiculous The patient shuffles along swinging his arms in an exaggerated fashion and advancing the toes only an inch or so with every step The feet are rapidly slid along the ground not lifted When the patient attempts to turn his tiny paces become exaggerated in rate though reduced in amplitude in a fantastic fashion

Senile disorders of gait from spinal lesions are probably rarer This statement holds true particularly if we except from this category what must surely constitute the most common cause—namely partial spinal compression from cervical spondylosis *Vertebral lesions apart spinal paraparesis* in the aged may perhaps also occur as a result of a senile combined sclerosis within the spinal cords of aged persons Perhaps that is to carry an attempt at pathologic precision too far

The muscles and tendons of the legs may themselves be the seat of advanced fibrotic changes to such a degree as to interfere with functional activity The central and peripheral nervous systems are not necessarily involved This is the condition which was originally described by Lhermitte under the term senile myopathy or myosclerosis and which resembles in many ways the clinical picture of dermatomyositis in younger subjects (2 53–55) Aged patients rendered bed fast by reason of some incapacity—cardiac or pulmonary perhaps—often slowly develop this myosclerotic contracture of their lower limbs The muscles become hard to the touch and somewhat tender and the overlying skin is bound down to the deeper tis

sues The muscle bellies and the tendons stand out conspicuously Gradually a flexion attitude of the legs develops and eventually becomes extreme Passive correction of the new posture is impossible even under deep anesthesia and active movements are considerably restricted Standing and walking are quite beyond the patient s capacity

This condition of progressive myosclerosis of the lower limbs is not at all rare and may be only too often witnessed in institutions for the aged or in domiciliary patients Immobility is the most important etiological factor, and this may be the consequence of neglect or inadequate nursing care Despite its common occurrence this syndrome has received scant attention in the neurologic literature

Senile muscular atrophy Within this category belong a number of ill defined conditions where localized muscular wasting shows up prominently against a background of a more evenly spread atrophy Involuntary movements may be visible which can be variously described as fibrillation or "fasciculation Usually the condition is intermediate between these two and the flickering shows itself particularly when the affected muscles are in active contraction as during the performance of a voluntary movement. Cramps are also a frequent complaint referred to the affected musculature and they may occur during states of rest (as in bed at night) or during activity

One characteristic variety of localized muscular wasting in the aged is to be found in the hand Most very old persons have a cert n thinn ng of ...

... But the clinical picture of a senile myatrophy of the hand is even more striking when fibrillation also occurs and when there are no gross changes in the metacarpo-phalangeal joints Sometimes the atrophy is limited to the muscles of the thumb as in the anterior tephromalacia of Marie and Foix (56) Lhermitte and his associates (57 58) have devoted much attention to this condition and to its possible pathogenesis They have raised the interesting suggestion that the group of nerve cells in the ventral cornua of the 6th and 7th cervical segments corresponding with the innervation of the thumb is in a precarious state as regards its arterial supply so that a senile endarteritis would easily lead to a local ischemia of that part of the spinal gray matter

age

sub ... the chief ... In some ways the clinical picture resembles that of motor neuron disease—especially the Aran Duchenne variety On the other hand it does not inexorably advance and lead to death from bulbar involvement More commonly it worsens only up to a point thereafter it

a step or two the legs may give way, the patient may stagger wildly, or one leg may cross in front of the other This is the "astasie trépidante" of the French neurologists, a variant is sometimes spoken of as Petrén's gait (48) Here the patient makes a few tiny steps and then comes to a standstill, with coaxing, however, he steps out almost normally. Again after a few paces he halts and is reluctant to proceed With further encouragement he starts again So it continues a few steps, and then a pause, and so on again

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The muscles and tendons of the legs may themselves be the seat of advanced fibrotic changes to such a degree as to interfere with functional activity The central and peripheral nervous systems are not necessarily involved This is the condition which was originally described by Lhermitte under the term "senile myopathy" or "myosclerosis," and which resembles in many ways the clinical picture of dermatomyositis in younger subjects (2, 53–55) Aged patients rendered bed fast by reason of some incapacity—cardiac or pulmonary, perhaps—often slowly develop this myosclerotic contracture of their lower limbs The muscles become hard to the touch and somewhat tender, and the overlying skin is bound down to the deeper tis

kind The patient usually denies having lost consciousness but it is possible that an extremely brief interruption in the stream of consciousness may have occurred without his knowing it

Giant-cell arteritis may well be included among the specific disorders of the senium which may present themselves as neurologic problems Headache is not a particularly common complaint in the elderly so that the appearance—late in life—of very intense neuralgia like pains localized within one area of the scalp should lead to the suspicion of a temporal form of giant-cell arteritis The adjective temporal is unfortunate for the arterial disease is often very wide spread and even when it affects the head it is not necessarily a temporal artery which is most involved (61) The diagnosis is not difficult being assisted by a conspicuous distension of the affected artery with exquisite tenderness upon handling Concomitant visual symptoms due to involvement of the retinal arteries are common There is generally a constitutional reaction with low fever malaise loss in weight eosinophilia and a raised blood sedimentation rate

The foregoing constitute the main specific neurologic affections of the sen —
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deg (o ro-ponto-cerebellar atrophy delayed cortical cerebellar atrophy) Pick s presenile dementia due to localized symmetrical cortical atrophy Alzheimer s psychosis paralysis agitans motor neurone disease and even some of the heredo-cerebellar ataxias It is not yet possible to account adequately for the selective decay of certain systemic or regional neuronic groupings in such conditions and naturally the hypothesis of a premature involution comes up for discussion This was specifically considered by Gowers who employed the term abiotrophy to apply to an inherent endowment of a limited viability to a particular part of the nervous system* Although Gowers ideas and also his term abiotrophy have come

*Gowers doctrine is so often involved and his original descript on so rarely quoted that t is perhaps des rable to reproduce some of the sentences conta ned in his lecture of February 21st 1902 (6) many of these parts have their own vital ty Some of them may slowly d e while the life of all the rest
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seems to halt, neither progressing nor regressing. Cases of this type were described long ago by Oppenheim, Michell Clarke (59), and recently by Neumayer (60).

Senile chorea deserves mention among the specific neurologic affections of the senium. Admittedly it is a great rarity, for one must be careful to exclude the possibility of a Huntington's chorea of unusually late development. Indeed we must at all times consider the possibility of there being a remote connection between Huntington's disease and senile chorea, and we recall *Haldane's suggestion that as the centuries go by Huntington's chorea* may be changing its natural properties by tending to show its first signs at a progressively later age.

Sufficient pathologic evidence exists to support the demarcation of a rare disorder of the senium characterized clinically by the late and gradual appearance of choreiform movements without any genetic properties and without any demential changes other than mild intellectual enfeeblement consistent with the patient's age. Such cases are attended on the pathologic side by neuronic outfall in the putamen and caudatum without any gross ischemic lesions and without any affection of the corpus Luysii or of the cortex (61).

Among the specific disorders of the senium we may also refer to one which embraces both neurologic and psychiatric features—namely Jakob's disease. This term is one which might be appropriately applied to the condition originally termed "senile Versteifung" or "senile Muskelstarre" (62). A condition of marked dementia occurring in the aged is associated clinically with severe extrapyramidal disorder. The neurologic picture is rather like that of Parkinson's disease *sine tremore* occurring in an unusually aged subject. From a pathologic standpoint there occurs nerve cell atrophy in the cortex and in the basal ganglia, especially the pallidum. Senile plaques are demonstrable within the globus pallidus.

Senile epilepsy includes a variety of disorders of consciousness which may first show themselves in the elderly. Convulsive manifestations are not always present, *and the term "senile syncope" might be preferable at times*. Patients differ according to the depth and duration of the disturbed consciousness, the circumstances under which an attack occurs, and the consequent subjective state. Temporary excitement and confusion may follow each episode, as in the variety of senile seizure specifically described by Barber (63). A broad distinction may be made between the cases which are of "cardiac" origin and those which are "cerebral" in type. In both cate

without experiencing any premonitory dizziness or warning of any or [illegible]

kind. The patient usually denies having lost consciousness, but it is possible that an extremely brief interruption in the stream of consciousness may have occurred without his knowing it

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The foregoing constitute the main specific neurologic affections of the senium It would be wrong not to refer however to the notion of a possible limited and also premature type of aging within the nervous system There immediately come to mind such conditions as the progressive cerebellar degenerations (olivo ponto-cerebellar atrophy delayed cortical cerebellar atrophy) Pick s presenile dementia due to localized symmetrical cortical atrophy Alzheimer s psychosis paralysis agitans motor neurone disease, and even some of the heredo-cerebellar ataxias It is not yet possible to account adequately for the selective decay of certain systemic or regional neuronic groupings in such conditions and naturally the hypothesis of a premature involution comes up for discussion This was specifically considered b[illegible]

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in for criticism, the notion cannot be carelessly brushed aside Gowers was very much alive to the speculative nature of his hypothesis and to the dangers of attaching a label to something imprecise and even nebulous We recall that the Vogts also later conceived of a 'pathoclisis to explain local tissue vulnerability

A correlation between the morbid anatomy of aging of the nervous system and the pathology of the hereditary ataxias has particularly attracted attention and more so in recent years Gowers paper on abiotrophy dates from 1902 (65) Raymond stressed the relationship between familial disorders and a premature localized senescence in 1908 (66) A similarity in the neuronic changes which occur both in aging and in the ataxias has been the subject of comment by Marinesco (67) Orton (68) and others In a recent symposium upon genetic disorders Schut (69) has drawn attention to a senile type of change in the skin of ataxic patients He believed that the facial expression matures early, and that some ataxic individuals appear older than their actual age Most clinical neurologists however, would hesitate to accept these views unreservedly

The doctrine of abiotrophy is, however, showing signs of being whittled away by advances in neurochemistry Thus the earlier views of Jelgersma (70) and Lewy (71) that Parkinson s disease can be looked upon as a pallidal involution is losing ground (72) Motor neurone disease is more and more under suspicion of being a toxic disorder of the spinal cord, rather than a primary degeneration

DISCUSSION

The foregoing account of the nervous system in the aged aims at bringing up to date our present knowledge of the subject inadequate though our ideas may be It would be unwise to close the discussion without indicating

name exists which we need frequently to speak of it is not wise I think to shrink from an attempt to give it a name Here the simplest mode of obtaining what we need is to insert the root of βιος after the negative particle in atrophy this gives us abiotrophy " But it is generally better if you can to appropriate what you need than to make it afresh and we find the word βιοτροφος used in the sense of vital nutrition If we prefix the negative particle we have the same word abiotrophy If a more general term is desired the adjective biotic has been occasionally used in English in the sense of vital and from this we may form abiotic to designate that which depends on defective vitality A corresponding substantive would be abiosis and this also has some warrant The word βιωσις was employed once or twice in old Greek meaning mode of life It is given us by the physician who is more widely known and esteemed on account of the character and precision of his writings and the devotion of his life than any other medical man who has lived—St Luke It is pleasant I think to take a word from him So I give you a choice of words by which to designate this unnamed conception

Subsequent neurologists seem however to have agreed in preferring Gowers first suggestion

the purely neurologic considerations where more data are needed and where there is promise of expansion in our understanding of old age in general

In the first place we need far more information as to the morbid anatomy of the senile nervous system Léri s monograph on the senile brain (73) and Sander s studies on the senile spinal cord (74) merely opened important chapters which are still far from being closed Though there have been many subsequent descriptive accounts of the pathology of the senile nervous system most of the cases studied have been examples of senile dementia and not of healthy old age In far too many cases information as to the patient s mental and physical condition before death has been quite inadequate We require much more knowledge about the changes in the nervous system which are compatible with normal old age—that is to say, subjects who have died at a great age from some non neurologic affection and who during life were in no way demented or psychotic.

The problem of the senile plaque is still of great interest to the clinicopathologic investigator Despite the considerable literature upon this subject we remain uncertain as to the meaning of these deposits—the ' black marks of old age as they have been called More information is needed as to the occurrence of these structures outside of the senium their precise, distribution within the nervous system and their correlation with chronologic age and with intellectual deterioration

Of great interest however is the belief that senile plaques may, in part at any rate signify the operation of a histochemical anomaly Divry (75) looked upon senile plaques as the expression of a disseminated hyalo-amyloisis affecting the cortex The traditional pragmatic attitude is therefore to regard them as evidence of a reactionary change directed against a specific metabolic process of toxic nature (76) First there occurs an involutional alteration in the chemistry of the ground substance embracing the neuronic elements In this way lipoid (or possibly amyloid) substances are precip [illegible]

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wh [illegible] ...logically by a profusion of plaques may be— to some extent at any rate—exogenous reactive or secondary manifestations of an aging process (a *senium ex morbo* rather than a *senium naturale*).

Special attention might also be paid to the involutional changes which can be found within the structures constituting the blood [illegible]

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and age and it is possible that evidences of aging are detectable here comparatively early. It is tempting to equate such changes in the plexus as occur with advancing years with a progressive inadequacy in its role as a filter or barrier.

Another histologic problem which still requires elucidation is one to which I drew attention 21 years ago (16). I refer to the differences in the nervous tissue reaction to a known noxa according to age. It would be a relatively simple matter and perhaps an illuminating one to compare and contrast the minute histologic changes within the cerebrum in cases of general paresis occurring in children, adults and the aged. Or the glial reaction around a tumor or a region of cerebral laceration might well be studied and documented with reference to the actual age of the patient concerned.

Yet another problem deserves detailed examination along both histologic and clinical lines. I refer to those rare but highly important cases of precocious senility met with in childhood. Although we are fairly well conversant with the skeletal, dental, dermatologic and endocrine reactions of these cases, we are still completely ignorant of the neurologic and neuropsychiatric aspects. We do not know, for example, whether such neurohistologic characteristics as senile plaques, Alzheimer's neurofibrillary tangles or the Bouman type of Purkinje cell change occur in cases of senium precox, progeria or even premature senility. We know nothing of intercurrent neurologic disease in such cases or indeed what constitute the clinical norms on routine testing of the nervous system. We know but little of the intellectual capacity of such patients or of their personalities or emotional life.

Let it not be asserted that discussion of this sort is academic or impractical. On the contrary, it is hard to conceive of a biologic problem which promises to be more utilitarian in its scope. It is to neurohistology that we look for information as to the relative importance of endogenous versus exogenous factors in the natural processes of old age. As already emphasized, herein lies the crux of the problem of extension of the life span and the preservation of mental and physical efficiency in the aged.

Although I have already used this quotation elsewhere (16), may I finish by repeating the words of Professor Tilney uttered in 1928 in New York.

Some day people will awaken to the fact that they have been missing the greatest constructive opportunities. . . . One liberally supported and effective brain institute *would prove an incomparably more profitable* investment for civilization than the most powerful battle fleet that ever sailed the seas. The political party which will have the foresight and humanity to

DISCUSSION

DR AUGUSTUS S ROSE [Los Angeles Cal] It is a privilege for me to open the discussion on this scholarly paper Although we are familiar with the richness of Dr Critchley's many writings there are many who will share my amazement in learning how much [illegible]

population is timely His paper will, without a doubt, become a reference of increasing importance for all students of the nervous system

It is unfortunate that time was not sufficient for Dr Critchley to complete the reading of his manuscript at this time The thorough coverage of the subject within the imposed limitations makes it difficult for the discusser to find an item of difference It is my desire, therefore, to emphasize and to stimulate further discussion

As a part of the presentation, Dr Critchley pointed out that the interpretation of the neurologic examination in elderly people may be considerably different from that of the average adult Wear and tear and the local effects of trauma, infections, and disorders of circulation and metabolism may cause the pupils, joints, tendons, and muscles to develop atrophies, rigidities, and contractures These changes interfere with the freedom of movement and may be confused with abnormalities in neurologic function

A problem of major extent is presented by the elderly person with muscle and joint disease giving a history suggestive of possible central nervous system pathology Minimal signs upon which we depend in the examination of younger people, may be masked These differences and difficulties in the neurologic examination of the elderly are important. However, it should be kept in mind that the neurologic functions which are tested by the usual clinical examination do not disappear because of age alone The absence of a tendon reflex or the failure of pupillary contraction may not be significant to the present illness but they are abnormalities which require assessment in the aged as well as in the young

With the tabulation and description of the neurologic disorders encountered in the aged, it is noteworthy that some type of alteration of the motor mechanisms accounts for the majority Tremors, rigidities, and disturbances in mobility are the hallmark of the aging nervous system yet, if a statistical measure were made, there can be little doubt that memory defects and a fixation of mental attitude would be as frequently or more frequently found It is said that aversion to change is the first sign of senility The aging person becomes set in his ways, and there is often an unreasonable resistance to, and frequently an inability to deal with, new ideas Can it be that this rigidity of mind like rigidity of the body, is a neurologic sign indicative of failure of neuronal function of the extrapyramidal system? A comparison of the mental status of elderly persons with and without the extrapyramidal syndrome might reveal interesting data in this regard

The nature of the aging process is a subject of considerable complexity, as has been attested to already in th [illegible]
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or abiotrophy [illegible] away by the advances of neurochemistry, and he stated that motor neuron disease is more and more under suspicion as a toxic disorder, rather than primary degeneration Since one of the most important questions in the treatment of chronic neurologic conditions rests upon the answer to this riddle, it would be

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Although I have already used this quotation elsewhere (16) may I finish by repeating the words of Professor Tilney uttered in 1928 in New York Some day people will awaken to the fact that they have been missing the greatest constructive opportunities One liberally supported and effective brain institute would prove an incomparably more profitable investment for civilization than the most powerful battle fleet that ever sailed the seas The political party which will have the foresight and humanity to introduce into its platform an article advocating and supporting the longer and better use of the human brain will offer a worthy issue to its electorate

Perhaps the most important fact that he brought out (and it was also emphasized by Dr Rose and is also applicable to the presentation by Dr Foley on vascular lesions of the brain) is that we may have to look outside the nervous system for some of these diseases that are usually considered to be neurologic. In arteriosclerosis the disease is generalized The changes in the brain are only a part of the picture Our primary problem is the cause of arteriosclerosis

Dr Critchley noted that some of the so called degenerative diseases, particularly Parkinson s disease may not be degenerative in nature I believe that as time goes on we can extend this concept even to Pick's and Alzheimer s disease, and that ultimately we will find that many of these conditions are not the result of premature death of the cell (because these were not born to live as long as other cells—the so called concept of abio trophy) b

psychiatrist and psychologist might have some answers to these things May I therefore, as a psychiatrist again make a plea for the understanding of the dynamic quality which is inherent in all symptoms in later life

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As I stated yesterday, I view these as dynamic processes and defensive maneuvers on the part of the ego As such they are not static phenomena but processes capable of re versibility It is this sort of belief which gives one courage and incentive to attempt ther apy in the aging person

Dr. Walter O Klingman [Charlottesville, Va] I would like to ask Dr Critchley one question I wonder whether in the pure form of senescence—and Dr Critchley said there are very few—there are any changes in the electrophysiology of the brain This problem has not entered the discussion as yet Are there any changes in the electroencephalogram? Are there evidences of an alteration of the normal patterns as the brain undergoes senescence?

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of great interest if Dr Critchley would give us the benefit of his own thinking in this matter

Specifically if involution and death are the natural and inevitable sequelae to growth and maturity in the cells and the cell systems can the process of involution be hastened differentially? And what are some of the factors acting in concert which may bring about slow premature death in some tissues without affecting others? If death can be hastened it should be possible to slow or alter its progression

In considering the neurologic disorders of the aged and asking questions concerning treatment we come to the basic matter of pathology What is actually to be found in the nervous system of a large number of persons dying in old age?

The Los Angeles Veterans Administration Medical Center, with which I have been associated in part during the past five years is a facility of approximately 7600 beds The 3800 beds in the domiciliary home are coveted by old soldiers from all parts of the country More than 80 per cent of the population of this unit are older than 60 years and there are at all times more than 300 individuals domiciled here who are older than 75 years

Recently my associate Dr Harry Fang with the assistance of the Medical Records Librarian reviewed the neuropathological findings in a series of autopsies performed at the L A V A Medical Center, for the purpose of answering the question, what is the frequency of primary and secondary disease of the nervous system in elderly persons and what is the relative importance of circulatory factors? These data may be summarized as follows

1 In autopsies performed on 130 patients 75 years or older from the General Hospital and Domiciliary Home during the year 1953 there were 92 with vascular lesions (softening 46 thrombosis 41 intracerebral hemorrhage 3 subarachnoid hemorrhage 2) 1 with degeneration of basal ganglia 3 with glioma and 31 with no neurological disease noted

2 In 95 consecutive autopsies performed on patients 70 years or older from the Neuro psychiatric Hospital between 1947 and 1950 60 were found to have cerebral softening 3 intracerebral hemorrhage 5 subdural hematoma 3 old neurosyphilis 5 degeneration of basal ganglia 1 meningioma 1 cerebral metastasis 17 no abnormality

These are impressive data they strongly indicate that vascular or circulatory disorders are demonstrable in the brains of 70 per cent of persons older than 70 years of age These figures would lead one to believe that future study might appropriately be directed first toward the blood vessels and the circulation of the central nervous system and their con tribution to cellular breakdown before accepting the concept that the aging process is a primary degenerative phenomenom

Dr H Houston Merritt [New York N Y] It is a great pleasure to have heard Dr Critchley and we wish to thank him for taking time out from other important obliga tions to attend this meeting He has in his comprehensive survey covered the subject of the neurologic abnormalities of the aged There are a few comments I should like to make in the way of emphasis

He spoke of changes that we find on routine neurologic examination in elderly patients I think he will agree that occasionally we will find in a man or woman of over 90 almost the same type of neurologic findings that we expect in a younger person

He emphasized that the usual changes that occur do not follow the phylogenetic hierarchy in that the newer system seems to be better preserved than the older ones The basal ganglia are particularly vulnerable and the symptoms that arise from presumed involvement of this structure are akinetic and amyostatic rather than hyperkinetic He emphasized the fact that in interpreting the examination of these individuals one had to consider structures other than the nervous system—that changes in the muscles and tendons and the joints participate in the clinical picture

Perhaps the most important fact that he brought out (and it was also emphasized by Dr Rose and is also applicable to the presentation by Dr Foley on vascular lesions of the brain) is that we may have to look outside the nervous system for some of these diseases that are usually considered to be neurologic. In arteriosclerosis the disease is generalized The changes in the brain are only a part of the picture Our primary problem is the cause of arteriosclerosis

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DR. JACK WEINBERG [Chicago Ill] I was interested in Dr Critchley s discussion of the posture of the neurologic older patient I was happy to hear him say that possibly the psychiatrist and psychologist might have some answers to these things May I therefore, as a psychiatrist again make a plea for the understanding of the dynamic quality which is inherent in all symptoms in later life

One must see the ag ng organism as being in a constant state of adaptation making constant attempts to adapt to an ever changing scene This adaptive ability obviously *requires energy* and energy is not easily available in later life. Adaptation requires not only perception and interpretation of that which is asked of the *organism but also* execution of an action All that requires an expenditure of energy one may see in the *aging organ sm* an attempt at conservation of this energy which may appear to the *observer* as *partial to total slo*wing down or an appearance of rigidity on the part of the aging patient.

As *I stated* yesterday, I view these as dynamic processes and defensive maneuvers on the part of *the ego* As such they are not static phenomena but processes capable of reversibility It is thus *sort of bel ef which* gives one courage and incentive to attempt therapy in the aging person

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DR D EWEN CAMERON [Montreal Canada] I would like to ask Dr Critchley three questions One of them has *been in* part at least asked by Dr Houston Merritt I would like to ask him about those *people* over the age of shall we say 70 who show very rapid movements who are quite capable of turning ...
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at 70 not ... ...ucuate in the last few days about the matter of what is really normal (and of course *by normal* we mean what is customary now) I suppose that the heights and weights of the normal of the average population are not those which were normal fifty years ago I would think that these people who can do things at 70 that most people cannot do at 70 might be looked upon perhaps as the prototypes of the future.

My second question is this I would like to ask about this business of bending down to pick up things Perhaps a decade or so ago I had a mentally alert elderly colleague He and I were putting on our rubbers preparatory to going out into the Montreal snows and he said Now look at this particular point you will see who is old and who is not because I have to hold onto something whereas you do not You just put your rubbers on and then put your finger in the back and pull it on

I don t think that this matter of holding onto something is tied up with rigidity I *think it is something else and I would like to ask Dr Critchley if he can comment on it* It is obviously different from the thing that the elderly wife complains about when she says I now have to lace up my old husband s shoes for him That I think is rigidity

The third question I would like to raise with him is this He talked about the sort of resistance which the old person had to even a passive movement and he offered several suggestions—in fact I was a little suspicious since he offered several as to whether any of them were really altogether satisfactory to him

I would like to add another possibility and have him comment on it if he will that is when you see an old person coming to you you may be reasonably sure that you are seeing somebody to whom nothing particularly good has happened for about ten years Nearly every change has been a change for the worse

These people have a much more pervasive attitude of anxiety and fear than most of us give them credit for I would be inclined to feel that that anxiety and fear are generalized over into almost every kind of change that you can imagine even into changes of posture and the like This then constitutes the third question as to whether we are really giving enough recognition to anxiety and fear as pervading almost anything a dose—the way he moves the way he turns around the way he steps out and walks

Dr MacDonald Critchley The changed attitude towards the so called abiotrophies is an important conception in modern neurology It is true that the evidence is not great and is largely based upon histologic similarity between toxic or metabolic disorders of the nervous system and the pathology of the so called abiotrophic disorders But I am sure *I am right in saying that many diseases formerly labeled abiotrophies are under suspicion* and they are gradually being whittled away one by one This is of course encouraging because it does offer a ray of hope in prevention and in treament

Dr Klingman has asked me about any specific alterations in the electrophysiology and whether they correlate with this dissolution process I don t know Dr Klingman I know that work is going on in various centers on this problem but I don t know what has been found

I quite agree of course that there are some old people who do not show slowness of movement and whose nervous system conforms to the normalcy of young adults

One of the difficulties in stooping and rising again in an old person is of course sluggishness of the vasomotor control leading to dizziness which at least is as important perhaps as rigidity

I am not sure about anxiety in old people as being an important factor in determining rigidity I have analyzed 252 old people who came to me aged 70 and over with relation to the nature of their symptoms and anxiety occurred in only 29 I should think that this rigidity, if it has to be correlated with anything psychologically is more likely to be correlated with mental viscosity and inertia rather than actual anxiety

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My second question is this I would like to ask about this business of bending down to pick up things *Perhaps a decade or so ago I had a mentally alert elderly colleague He* and I were putting on our rubbers preparatory to going out into the Montreal snows and he said Now look at this particular point you will see who is old and who is not because I have to hold onto something whereas you do not You just put your rubbers on and then put your finger in the back and pull it on

I don t think that this matter of holding onto something is tied up with rigidity I think it is something else and I would like to ask Dr Critchley if he can comment on it *It is obviously different from the thing that the elderly wife complains about when she* says I now have to lace up my old husband s shoes for him That I think is rigidity

The third question I would like to raise with him is this He talked about the sort of resistance which the old person had to even a passive movement and he offered several suggestions—in fact I was a little suspicious since he offered several as to whether any of them were really altogether satisfactory to him

I would like to add another possibility and have him comment on it if he will that is when you see an old person coming to you you may be reasonably sure that you are seeing somebody to whom nothing particularly good has happened for about ten years Nearly every change has been a change for the worse

These people have a much more pervasive attitude of anxiety and fear than most of us give them credit for I would be inclined to feel that that anxiety and fear are generalized over into almost every kind of change that you can imagine even into changes of posture and the like This then constitutes the third question as to whether we are really giving enough recognition to anxiety and fear as pervading almost anything a dose—the way he moves the way he turns around the way he steps out and walks

Dr MacDonald Critchley The changed attitude towards the so called abiotrophies is an important conception in modern neurology It is true that the evidence is not great and is largely based upon histologic similarity between toxic or metabolic disorders of the nervous system and the pathology of the so called abiotrophic disorders But I am sure I am right in saying that many diseases formerly labeled abiotrophies are under suspicion and they are gradually being whittled away one by one This is of course encouraging because it does offer a ray of hope in prevention and in treament

Dr Klingman has asked me about any specific alterations in the electrophysiology and whether they correlate with this dissolution process I don t know Dr Klingman I know that work is going on in various centers on this problem but I don t know what has been found

I quite agree of course that there are some old people who do not show slowness of movement and whose nervous system conforms to the normalcy of young adults

correlated with mental viscosity and inertia rather than actual anxiety

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dures are the same as for younger patients, it is only the tempo that is dif erent. Hemiplegia is an excellent example

HEMIPLEGIA

One of the most significant disabilities in terms of the numbers of pa tients seen by neurologists is hemiplegia usually the result of brain damage following thrombosis embolism hemorrhage, or trauma There are no definitive statistics available on the number of hemiplegics in the United States but estimates have been as high as 1 800 000 (2)

Some idea of the magnitude of the problems may be gleaned from the fact that stroke is listed as the third major cause of death in the United States ranking behind only heart disease and cancer Even so the ma jority of patients sustaining a stroke of apoplexy do not die from the initial insult. Instead they improve to a greater or lesser degree, and often live a number of years despite their residual disabilities

The diagnosis is not difficult but in the past unfortunately, the medical attitude toward the hemiplegic has been one of hopelessness and passive acceptance. Such patients in municipal hospitals and chronic disease in stitutions have always posed serious disposition problems and have crowded the few nursing homes and institutions for custodial care Usually they re

... chronic custodial cases of which 36 were hemi plegic it was found that only seven of the 95 were in need of continued hospitalization (3)

In the hands of the physician trained in rehabilitation and the rehabilita tion minded neurologist the hemiplegic is not a lost cause and 92 per cent of the proper... urinary and ... tion 30 per ... be taught to do gainful work, usually in the fields related to previous work experience Further evidence of the value of dynamic rehabilitation services has come from a carefully controlled study in which objective quantitative analysis of comparable groups of patients indicated that a retrained group demonstrated over 130 per cent more gain in activities of daily living than did an untrained group (4) The return of range of joint motion and muscle strength were also more pronounced in the retrained group although the increments were not as striking as in the activities of daily living

In training the elderly hemiplegic it is important that in the early weeks of the disability as much of the training as possible be done at or around

CHAPTER XIV

REHABILITATION OF THE ELDERLY NEUROLOGIC PATIENT

HOWARD A RUSK

Through the years the neurologist has been considered by his colleagues to be the great master of finite diagnosis a skill that has required not only the most complete knowledge of neuroanatomy and neurophysiology but infinite patience and skillful deductive reasoning In the past however a great number of neurologic diseases were considered to be hopeless once the diagnosis was established for the etiology was unknown and the therapeutic tools were few and far between

Although many neurologic conditions are still enigmas today the attitude has changed Even though there are but few specifics the neurologist recognizes that many of his patients can be materially helped with the tools of modern rehabilitation Leadership in the field of neurologic rehabilitation has come from both the neurologist and the specialist in rehabilitation There are numerous examples of substantial even dramatic results where these tools have been vigorously used

Soon after World War II such a program was inaugurated at the Veterans Administration Hospital Minneapolis for 130 chronic neurologic patients all but two of whom were veterans of World War I and many of whom had not been out of bed in 10 years After 9 months of rehabilitation 25 had left the hospital and were employed and 10 others had been discharged to their own homes capable of light work Of those remaining 30 were ambulatory and undergoing advanced rehabilitation and 25 were capable of some self care All but ten of the group had shown some worthwhile permanent improvement (1)

Rehabilitation is a teamwork job not only in name but in operation In our own services at the New York University Bellevue Medical Center the Physical Medicine and Rehabilitation Service work hand in hand with the Neurologic Service exchanging residents joining in common rounds and participating in patient seminars together All in all it has been not only a

his family and the community

The subject of our discussion today is that of rehabilitation of the elderly patient In the rehabilitation management of the elderly patient the proce

can usually be lengthened by means of stretching and a short leg brace with a 90 to 110-degree stop at the ankle to maintain the gains made by stretching and ambulation

Flexion and extension movements at the hip and knee can usually be performed by the spastic hemiplegic subject who is started on early ambulation When however, the hip and knee are flexed, as in walking, the foot dorsiflexes and supinates The patient is usually afraid to place the supinated foot on the floor because of instability To prevent this, he walks with a fixed knee joint and circumducts the lower extremity This is a slow, awkward gait and, if used for a period of time, the patient develops *a pattern of* walking that is cumbersome, fatiguing and difficult to correct

A double bar, short leg brace with a stirrup attachment, 90-degree ankle stop and a supinator T strap should be prescribed to prevent plantar flexion and supination of the foot and give the patient confidence so that he will flex his knee and hip With the brace, and a cane in the unaffected hand for balance, most hemiplegics soon learn to walk unassisted

As a return of function in the affected upper extremity is usually very slow it is essential to teach the patient to care for his daily needs with his unaffected arm

A right hemiplegia in a right handed person is an especially serious dis ab [illegible]

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tl [illegible] be started early, as the patient must become left handed if he ever hopes to care for his daily needs Simple tasks in eat [illegible] and dre [illegible]

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The fingers of the spastic hemiplegic patient are most difficult to re educate for useful purpose If adequate function is attained, it takes a great deal of time and concentrated effort by both the patient and the therapists

In the rehabilitation of the hemiplegic, it is readily apparent that numerous factors will determine the degree of results obtained in ability to perform the activities of daily living Some patients will achieve a surprising degree of recovery of function others will be [illegible]

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the bed for in this period there is still localized edema with continuing confusion Even a move toward the end of the ward can on occasion be a confusing and disturbing experience Here again the general rules for the management of the elderly patient must be fitted to the rehabilitation training program

The objectives of a program of rehabilitaiton for the hemiplegic patient are 1) to prevent deformities 2) to treat deformities if they occur 3) to retrain the patient in ambulation and elevation activities 4) to teach him to perform the activities of daily living and to work with the unaffected arm and hand 5) to retrain the affected arm and hand to its maximum capacity, and 6) to manage facial paralysis and speech disability if present (5)

The ordinary spastic hemiplegic when lying in bed holds the upper extremity in abduction and internal rotation with the elbow wrist and fingers of the affected part in a flexed position The affected lower extremity *is usually flexed at the hip joint the knee is flexed and the ankle is* plantar flexed and supinated

If an active program is started within a few days following the cerebrovascular accident there is no need for any special procedures to protect the affected limbs If however the patient must remain in bed for a period of time procedures must be instituted to prevent deformities

A posterior half shell lower extremity splint is used to prevent shortening of the heel cord A pillow in the axilla and sandbags laterally will prevent abduction and rotation of the shoulder joint a frequent residual deformity in hemiplegia Passive movements of the arm in abduction external rotation and in the overhead position should be performed several times a day to prevent a frozen shoulder

The principal deformities that may occur are a frozen shoulder and short heel cord The use of heat and massage to the arm and shoulder are of value in preparing the part for stretching Passive movements of the shoulder are useful in increasing the range of motion

The use of pulley therapy to prevent shoulder ankylosis will also aid in the development of reciprocal patterns in the upper extremities This can easily be managed with the use of a modification of an overhead frame a window *pulley and a length of clothesline* Experience has shown that the relative return of function in the affected arm is usually less than in the involved leg Coordination exercises may be helpful but emphasis should be placed as early as *possible on the use of the unaffected arm* this is especially true of the relatively young patient In addition a triangular arm sling should be used to elevate the affected arm This is of aid in minimizing localized edema and in preventing shoulder subluxation

A short heel cord seldom requires operative procedures The heel cord

can usually be lengthened by means of stretching and a short leg brace with a 90 to 110-degree stop at the ankle to maintain the gains made by stretching and ambulation

Flexion and extension movements at the hip and knee can usually be performed by the spastic hemiplegic subject who is started on early ambulation When however, the hip and knee are flexed as in walking, the foot dorsiflexes and supinates The patient is usually afraid to place the supinated foot on the floor because of instability To prevent this, he walks with a fixed knee joint and circumducts the lower extremity This is a slow, awkward gait and if used for a period of time the patient develops a pattern of

...ion and supination of the foot and give the patient confidence so that he will flex his knee and hip With the brace, and a cane in the unaffected hand for balance most hemiplegics soon learn to walk unassisted

As a return of function in the affected upper extremity is usually very slow it is essential to teach the patient to care for his daily needs with his unaffected arm

A right hemiplegia in a right handed person is an especially serious disability because of the sensory and motor aphasia and the lack of skill in the left hand to perform the activities essential for daily living The training of the left hand should be started early as the patient must become left handed if he ever hopes to care for his daily needs Simple tasks in eating and dressing should be started Left hand writing must be practiced as this is an important means of communication—especially when speech is affected

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The fingers of the spastic hemiplegic patient are most difficult to reeducate for useful purpose If adequate function is attained it takes a great deal of time and concentrated effort by both the patient and the therapists

In the rehabilitation of the hemiplegic it is readily apparent that numerous factors will determine the degree of results obtained in ability to perform the activities of daily living Some patients will achieve a surprising degree of recovery of function others will be left with ...
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to perform many acts of daily living either independently or with a minimum of assistance from another person Such devices should be used only when necessary and before a device is given to a patient retraining in the activity is a necessity

One of the most difficult problems in the management of the hemiplegic is the problem of aphasia It is extremely important for the physician to explain both to the patient as soon as he is conscious and to his family what aphasia is and why the patient is unable to speak Simple as such a procedure is it is commonly overlooked This should be done as soon as the patient has recovered consciousness and aphasia is noted in order that his fear of losing his mind may be allayed he can be told factually and honestly that there is no specific medical therapy for aphasia and can be impressed with the necessity for retraining

We have recently had an interesting experience in the management of hemiplegia in our own department (6) Birch attacked the problem by attempting to modify the *block* rather than accept the theory of subtraction He chose 14 aphasic patients who had been under therapy for six months or longer and who had a vocabulary of less than five words By giving them a shocking dose of sound he found that in a matter of seconds their vocabulary increased from 12 to 15 words and by continuing the shock over longer periods of time gains could be increased and maintained More than 80 per cent of the initial group were trained to the point of an adequate vocabulary for daily use While the series is far too small for any conclusion it certainly presents an interesting approach to a most difficult problem

Hemiplegia presents one of the most challenging problems in medicine today in both total numbers and therapeutic complexities With a dynamic approach to the problem of the hemiplegic using rehabilitation techniques that have been developed to meet the total needs of the individual much can be offered to these severely disabled patients and many can be trained so that they achieve lives of self sufficiency and usefulness

One of the great neurologists of our time Spiller gave one of the therapeutic keys to modern rehabilitation when he said Action absorbs anxiety Directed action does more than absorb anxiety It can provide the tools for learning that can take a surprising percentage of even the elderly neurologically handicapped back to lives of comfort and self care and many back to gainful occupations If one word could be used to designate the therapeutic goals in such a program it would be the attainment of dignity

DISCUSSION

Dr Pearce Bailey [Bethesda M I] Dr Rusk the outstanding leader of the modern dynamic movement in rehabilitation has discussed the role of the neurologist as a diag

nostician and also the broader therapeutic role that clinical neurologsits are assuming in medical practice

We might say that the expansion of neurology in the last five years may be attributed to three major developments in this field, one being the discovery of new medications for the control of certain neurologic disorders, such as epilepsy and myasthenia gravis, the second being the discovery of vast new reseatch vistas in experimental neurolgy, particularly in the areas of neurphysiology, biophysics, and biochemistry, and the third being the gradually growing interest of neurologists in assuming a long time responsibility in programs for the care of chronic neurologic patients, for whom no specific treatment is known

With this movement has grown a considerable expansion of neurology, particularly through training grants programs, which have been developed and supported by the National Institute of Neurological Diseases and Blindness While this training grants program is currently only in its second full year, as a growing project which requires at least five years for any definitive evaluation, yet certain preliminary spot observations already have been made a general improvement in the quality of neurologic training 50 *per cent more neurologic residents in training now than two years ago* and more than 100 per cent increase in the number of medical schools having established graduate training

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The future training of clinical neurologists who wish to assume responsibility in the total care of their patients must extend, therefore beyond the methodology of the routine neurologic examination, for instance, additional emphasis must be placed on training in ...hniques for the determination of the patient s present and potential capacity to develop ...eful neuromuscular patterns Such a program also calls for the neurologist to broaden ...sights for a fuller comprehension of the patient s needs, not only in relation to the ...aluation and care of his neurologic disabilities as a hosp...

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...on ... The first is how can we improve—and this is the business of all researchers—the methodology for the evaluation of the rehabilitation of chronic patients? It is obvious that the existing accepted methodologies of natural science and empirical methods must be revised if we are to apply the results of basic ... bilitation of chronic patients.

The second matter is one of a professional dichotomy which exists to a certain extent, and even larger than I had thought previously, after haveing attended a meeting on the problem of neurological disability as a public health question under the auspices of the National Public Health Council last week in Arden House, Harriman, New York The dichotomy comprises the physician, on one hand, and the professional personnel concerned with the educational, psychologic, social, and economic adjustment of the patient, on the other Where do the responsibilities of medical rehabilitation end? Where is the line of demarcation, between medical and social or educational rehabilitation, or should there be no line of demarcation, and should it all be included under the caption of medical rehabilitation?

DR AUGUSTUS S ROSE [Los Angeles, Cal] Our experience in Los Angeles in rehabilitation has been primarily directed toward the epileptic I would like to comment in this connection that the rehabilitative method has been used by taking advantage of subcontracts from industry and paying the patients an actual wage These individuals are those in the domiciliary unit of the Los Angeles Veterans Administraion facility They represent the extremely disabled The majority are domiciled for life Convulsive seizures have been poorly controlled despite attempts with all forms of medication They are difficult personalities, and many of them have not had remunerative work in any form for many years Most of them have lost self esteem and any feeling of being a part of the community

This experience has demonstrated a number of very satisfactory results, among the most important of which is the gaining of self assurance by the individuals and a feeling that they are a citizen again Seizures improve without change in medication They stop complaining about health and living conditions The jingle in the pocket seems to us to be an important motivation In fact, in these individuals the desire to have an income is of such importance we wonder if it shouldn t be utilized when possible in all rehabilitation efforts

DR MABEL ROSS [New York, N Y] May I thank Dr Rusk for pointing out that rehabilitation true rehabiltation means training in relation to the realities of the life that the individual is going to live later There is, it seems to me, some danger of substituting the Golden Age Clubs for real rehabilitating programs, because they are so much easier

Age Club to satisfy the needs of the older people in the community is too much like assuming that giving children many toys will substitute for real attention on the part of their parents

DR WALTER O KLINGMAN [Charlottesville, Va] I would like to reemphasize what Dr Rusk has already mentioned namely that in one segment of our society, that is, the veteran, this matter of care for the aged has became a problem of tremendous proportions We are already facing it There is no need in deluding ourselves about it It is here

I think that Dr Rusk has pointed the way and spearheaded one means of approaching this matter that has proved to be successful In the meantime of course, as he points out we hope that something can be done in the way of helpful investigative work and research work I am sure that he could have told us many more interesting things about the adjuncts in the care of the aged that apply more particularly to neurological disorders

but it is a costly matter that will affect the taxpayers particularly in housing these in dividuals. It is a very refreshing thing if you visit some of these installations where veterans have been around for years and years and suddenly an individual joins the staff who provides motivation and a goal I must admit they don t all have the dynamic personality of Dr Rusk but driving force is a tremendous help in reducing the hospital population and the cost to the public.

DR. JOHN WHITHORN (Baltimore Md) It has been a pleasure today not only to listen to Dr Rusk but also to observe the eagerness and enthusiasm shown by this audience With persons who start such a major revolution in medicine as Dr Rusk has done, we are historically accustomed to expect them to be disturbing persons likely to arouse opposition to have to hit hard in order to produce effects This has been an extraordinary phenomenon in the last decade—to see how Dr Rusk has brought about this change or at least started it on its way and has maintained so good a rapport and so warm a welcome within all the medical groups with which he has come in contact

I suspect that there is a reason for this and I think it lies in the nature of his appreciation of motivation in the very persons for whom he has been eager to carry out rehabilitative procedures in his recognition of the motivations in the professional groups whose outlook and habits he has undertaken to change and in the extraordinary way in which a team engaged in rehabilitative procedures supplements and evokes motivation of the patient I would like it very much of he would comment on his view of motivation in rehabilitation

DR. ERNEST M GRUENBERG (New York N Y) I would like to comment on one point that Dr Rusk made regarding the well known phenomeon of reduced anxiety in the aphasic patient When you tell him your diagnosis tell him that you have seen this disorder before and that you know something about the anxiety produced in him

It seems to me that this very vivid description that we have heard raises the problem as to what the psychologic effect of doctor patient communications in the chronic neurologic diseases of the aged represents to the patient I think this highlights the obvious fact that what the doctor says to his patient makes a difference to the patient and what the doctor thinks is wrong also makes a difference so that our diagnosis is tremendously important. Whether one views some of the symptomatology of the aging person as Dr Critchley does in his masterful clinical description of the symptoms that we see or whether one views them as Dr Weinberg does as psychologic defenses in the old person makes a great deal of difference as to what the doctor is going to sa

If we [illegible]

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[illegible] not advocating any particular answer regarding any particular symptom but it seems to me that we should be conscious of the fact that what we think is the cause of the symptoms we see in the older person will make a difference in what that patient will have to do about it

DR. HOWARD RUSK I have been given questions that would take until late afternoon to develop but I will try at least to give off the cuff rapid answers

I appreciate Dr Pearce Bailey's comment and I also appreciate his great understanding and help throughout the last decade when we have worked together There has been a time when there has been a lot of misunderstanding about where rehabilitation starts and where the other stops etc. It doesn t exist any more A neurologist makes a wonderful

head of a rehabilitation program if he is interested in this phase of the program and wants to take the extra time for training. The training goes hand in hand in our own institution. Residents are exchanged; rounds are common. This is a thing we do together, and if we all did ten times more than we are able to do, there still would be a terrific shortage of services.

There is great need to improve methodology for evaluation, and one of the most difficult ones is in the cardiac. We don't know, except *with rough clinical tools, how much* a man can do. There are no energy studies that are satisfactory. Clinical evaluation is crude. Recently in our own clinic we had an individual to fit with prosthesis. He was a cardiac and he was decompensated. We asked that he be sent back when he was compensated and ready to learn to walk. He came back four months later, after care in a clinic of excellent quality, and he was said to be ready for rehabilitation. He stood up on his one leg to have his stump measured and fell dead in the evaluation clinic.

We could look to magnificent services like Vauxhall in Great Britain, where they have done such great work in fitting machine to man and man to machine. In a civilization that can develop the electronic and atomic age, certainly these problems, if we turned our attention to them, would not be too difficult. But we have to go far beyond the faltering steps we have taken.

As to dichotomy, this is a total program. It starts as a medical rehabilitation program. That is the first phase of total rehabilitation, and at that time the doctor and only the *doctor is responsible for the entire training program, the emotional evaluation, the rou*tine for prevocational evaluation, the problems in social adjustment and social necessities. But then, when you get to a certain phase, the major need of that individual is the social and the vocational—but always the medical continues. It is just like a patient who is over an acute illness but has a continuing medical situation which you must follow throughout the years. It will not be primary or acute, but you must always be there; you must always be the figure that joins that individual to home base.

In a very careful follow-up study we found that the great mistake in our program had been in not continuing the relationship that goes on indefinitely with the discharged patient, because the results are entirely different if you have it; they need the security of belonging.

I could not agree more with Dr. Rose about the necessity for the individual to be able to make some kind of material gains by working, in spite of his disability. Four years ago a bilateral amputee who had been running our job placement experimental program de*cided that he wanted to go into business. He borrowed $8000 from eight individuals* and he started an assembly plant out in Hempstead, with the ground rules that you could work there only of you were beyond the age of 60 or if you had a severe disability. It is now in its fourth year and he has 170 employees. It is known as Abilities, Inc. They have Blue Cross health insurance, group life insurance, and a dynamic recreation program. When I say "disabled people," I mean twenty paraplegics, several blind and deaf. The head of the shipping department is a quadruple amputee. That is the type I am talking about. They now have set aside enough money to build a new plant, with more than $150 000 earned in the last four years, to enlarge to 500, and they have enough contracts that they have gotten in competitive bidding to last them for five years.

The reason is simple. These people are dedicated. It is their job. It is their life. It is their love. It isn't just a 40 hour week and a pay envelope.

The old age clubs fill only a part of the needs: ice cream when you need bread and meat. There are fourteen million individuals in the United States today beyond the age of 65. One third *have no income* at all, one third have less than $500 a year, the remaining third are self employed to the extent of 50 per cent. We have to find some means whereby

these individuals, within their tolerance, can work and have the opportunity not only to eat and exist, but to purchase their necessities

As to motivation, the greatest tool to motivate is opportunity and the stimulation of working with others who have the same problem, who are in various phases of conquering their disability

Our problem at the instant is not one of motivation It is a matter of keeping the patients from working too hard and too fast Also I do not believe there should be segregation of paraplegics and hemiplegics and multiple sclerotics and amputees and the young and the old This is a total program The quadriplegic is glad he does not have a disease like multiple sclerosis and the multiple sclerotic is glad he is not a paraplegic, and the hemiplegic is glad that he has one leg and has not lost two Patients are incomparable teachers they are the yeast in the fermentation of motivation My teacher in neurology, Dr Spillen said three words that I shall never forget "Action absorbs anxiety" Action also generates motivation

I close with one word that is one of gratitude to you in neurology and in psychiatry for your understanding and help in this program, without which it never could have been successful. Thank you

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CHAPTER XV

PANEL DISCUSSION

The Physician's Contribution to the Role of Older Persons in Society

INTRODUCTION

President Moore The afternoon session will be devoted to a panel discussion on "The *Physician's Contribution to the Role of Older Persons in Society* The chairman of the panel is Dr D Ewen Cameron who will introduce the members of his panel and describe the system of operation

Chairman Cameron Perhaps I might, first of all make some statement about the general purposes of the panel and then introduce the panel members

The general purpose of the panel is to discuss a very important factor in our society that fact being that the older person is now seeking to define his place in the community He has been displaced from his position as a craftsman the master worker or the old man of the family Methods of production have dispossessed him and our rural urban shifts have taken him away from the fireside which he used to occupy He is really the social isolate of our times

There are now too many of him and too few of the old positions which he formerly occupied for him readily to find a suitable place a satisfying place in our society He is now seeking his new role and our communities have the responsibility and also the pressing need of self interest to help him find it

As part of our society and perhaps having a particularly large share of the relevant facts the physicians have to help him and support him in the new role into which he is moving This then is a task that the members of the panel have before them today to explore with you the various ways in which we can contribute to supporting the old man in his new role The support reaches all the way from aiding him through acute break downs to clarifying the preparation for retirement and combating fallacious anticipations of what the aged person can do and finally helping him in his rehabilitation

I am going to introduce to you now the members of the panel The first one on the program is Dr Eugene Meyer who is Associate Professor of Psychiatry and also Associate *Professor* of Medicine in Johns Hopkins Hospital where he is in charge of the psychiatric liaison service The next on the list is Dr James S Tyhurst who is Assistant Professor of Psychiatry at McGill University He is in charge of the field studies carried on by the Gerontological Laboratory in the Allen Memorial Institute The next is Mr D S Sargent who is the Personnel Director for Consolidated Edison He has had a long experience in the personnel field and has been particularly concerned with problems of retirement and disability Dr David Seegal is Professor of Medicine at the College of Physicians and *Surgeons* Dr Margaret Mead unfortunately is ill Her place has very kindly been taken on short notice by Dr Rhoda Metraux who is an anthropologist and at present a re- [illegible] fellow at Cornell University Medical School Dr Jack Weinberg is Clinical Asso

[illegible]

Reese Hospital And finally, Dr [illegible]

Home for Aged and Infirm Hebrews of New York

With regard to the operation of the panel each panel member will outline in general his participation in the panel so that you may identify his field of interest Then we will have questions from members of the Commission and from members of the panel Members of the audience may if they wish pass up written questions which can then be put to the members of the panel.

I will now call on the first member of the panel to open the discussion Dr Eugene Meyer who will speak on Acute Breakdowns

1 ACUTE BREAKDOWNS

EUGENE MEYER

The study of acute psychologic breakdown at any age involves a multiplicity of factors In the patient these include 1) genetically determined potential 2) early life experiences with special reference to those that create serious impairment or rigidity in ego function 3) acquired habits, satisfactions and successes in mastery of the environment 4) the current flexibility and range of inner emotional response available to the person, and 5) the environmental opportunity, current and in the expected future for obtaining emotional satisfactions and maintenance of self-esteem

All these issues are relevant to acute breakdown in elderly persons and it is clear of course that all of them need much further study and research One must then ask whether there are special or unique features to acute psychologic breakdown in elderly people Two aspects of the elderly person's situation are generally mentioned The first is the different social economic and family status Certainly these differences in status as a productive person and as a significant member of the family would appear to have relevance to the motivational patterns in convalescence if not to the precipitation of acute psychologic breakdown But just because there are definite problems for elderly people in the structure of social economic, and family life we must be all the more alert to the fam[illegible] danger of appl[illegible]

[illegible] acute psychologic breakdown Certainly in our own psychiatric consulting work in a general hospital we have repeatedly found ourselves making all too-easy assumptions about the role of the [illegible] ess and [illegible] this mar[illegible] of inter[illegible] [illegible] in resort to various stereotyped self justifications for having done a less good job

The second factor most commonly referred to in elderly patients is that of impairment of brain function due to arteriosclerosis or senility It is worth distinguishing first of all between deficit situations or impairments of physical and mental functioning and acute psychologic breakdown. Metabolic imbalances deficiencies in oxygen supply to tissues in

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thing is different in the acute psychologic breakdown in elderly people it is apt to be a particular concentration or coalescence of multiple internal stresses and impaired adaptive responses In fact, however, we have no thorough knowledge of how such a special concentration of factors may operate in the precipitation of acute breakdowns in elderly persons One fact we can observe, however, is that this concentration of factors is operationally important in eliciting attitudes of pessimism, if not avoidance and despair, in persons who have significance and meaning for the elderly person at the time of the acute breakdown—and among these persons we must number the physician, himself Study of the precipitation and recovery processes in acute psychologic breakdown in older persons must include study of the physician's inheritance of our culture's definition of the role of older persons and the effect in turn, of these attitudes on the older person's experience during the acute breakdown As psychiatrists we have a special debt to those physicians who have consistently interested themselves in the aging process and in the psychotherapy of older persons They have shown that not only is there reason for therapeutic optimism, but that as physicians and psychiatrists interested in human functioning we often neglect an area of clinical research which is full of significance and interest for the understanding of all human behavior

2 RETIREMENT

J S TYHURST

The remarks that follow are based upon the research we are doing currently This consists of a study of retired people living in the community

We have attempted to study the process of retirement without primary reference to mental health concerning ourselves with the way in which the people whom we are studying have met the problem in terms both of their expectations and of their subsequent adaptation

The first question we must ask is, 'What is the meaning of retirement?'—that is what sorts of meaning does retirement have to a person who is retiring

One way of looking at it is to call retirement simply an example of *change or transition* regardless of the particular content involved In our case the transition is retirement from work The concept of transition brings it into line conceptually with other stages of transition in life [illegible] as adolescence [illegible]

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cluding the brain, and acute insults to brain function do not necessarily produce neuroses or psychoses. Moreover, no one has shown by valid evidence that acute reactions of delirium are in fact less reversible in elderly people than in younger people. When there is a temporal association between organic impairment to psychologic functioning and psychologic breakdown there is no correlation between the extent of organic and physiologic impairment and the degree of psychologic breakdown. As in the so-called "traumatic neuroses," minimal physical insults or impairments in elderly people can be associated with severe acute psychologic breakdown and very severe physical impairments may result in minimal or no psychologic breakdown. Deficit situations in elderly people, so commonly associated with arteriosclerotic change in the brain, may produce impaired capacity to cope with the physical, working, and family environment. But it is the elderly person's internal perception of the deficit and the personal meaning of the deficit in terms of that particular person's life that determines whether or not acute psychologic breakdown will occur. Kurt Goldstein's conception of the catastrophe reaction is particularly helpful in understanding this matter.

Thus impairments of sense perceptions and impairment of their integration into patterns of meaning may be less important than the feeling of sudden and strange distortion of body ego. Thus the threat to the person's role (as breadwinner, head of a family, and a member of society) may sometimes be realistic, but it is also often a highly exaggerated and dread-tinged version of what the future will bring. Thus sudden physiologic impairment may produce a severe abrupt loss of self-esteem and evoke depressive reactions accompanied by various degrees of agitation. But the threat to self-esteem is also related to the lifelong personality structure and values and may be entirely out of proportion to the real capacities for mastery. Finally, it is well to remind ourselves that in the older person as well as the younger person the sudden onset of physiologic impairments may provoke intense fear of being overwhelmed by previously repressed instinctual drives, both sexual and aggressive. Even very minor degrees of physical and physiologic insult can produce a state of panicky apprehension of lack of control not only of the external environment but of the inner instinctual forces.

In summary, when taken *separately* the significant issues in acute psychologic breakdown in elderly people are in no way different from the significant issues of acute psychologic breakdown in younger age groups. One might add that impairment of environmental mastery is a characteristic problem in many chronic illnesses. A catastrophic reaction to sudden insult to the central nervous system occurs in all age groups. Severe degrees of social isolation are by no means peculiar to older persons. If any

buy their way out of any other problems that may arise The data so far do not bear this out, and suggest that exclusive emphasis upon the importance of financial planning is a mistake While an increase in pensions is needed everywhere no amount of money can deal with many of the problems faced by the retired

A sixth meaning of retirement may be based upon the resulting change in *social status*—that is the place in a particular system which a certain individual occupies at a particular time [1] In our society, the fact that an individual works gives him a certain status in his family and in other social situations Furthermore his status in the particular occupation or institution is itself an important source of satisfaction and self esteem Retirement may therefore mean not only the loss of status with respect to the occupation itself but secondarily it may (and often does) mean a loss of status in other areas of activity and participation in our society The position as head of the family may pass to one of the children or even to the wife The retirement from occupation may signal the transition from the "useful to the useless from a functioning member of a work-oriented society to the status of an unoccupied aged person

A seventh view of retirement comes when one recognizes that the concept of status becomes psychologically significant when viewed in terms of *social role* Again for purposes here we might use Linton s definition the sum total of the culture patterns associated with a particular status It thus includes the attitudes values and behavior ascribed by the society to persons

All these ways of viewing retirement are probably relevant at various

social change In doing this we need to extend studies of transition made in respect to disaster and migration and particularly to study the natural history of the process of retirement in the same fashion as we have studied the natural history of disaster and migration we ha

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[1] Here we would agree with the definition provided by Linton who extends the notion of status beyond position in the prestige system of the society to include position in each of the other systems

We have had an opportunity, by means of intensive case studies to formulate the way in which the individual characteristically meets problems involving change or transition That is one way of conceptualizing retirement.

A second way is to consider retirement as a situation of *bereavement or grief* This immediately puts us in touch with a very wide range of material already in the literature—the ways in which these states can be dealt with through individual grieving and through institutional or social rituals in our society that assist a person through the bereavement transition There is little ritual at present that enables a person to go through the particular bereavement of retirement.

A third meaning that retirement may have is *loss of activity* This conception of retirement is based upon the view that some form of activity is necessary for satisfactory adaptation The emphasis is essentially upon activity as such and sees the problems posed by retirement as essentially those of physical and mental inactivity We have not found this point of view too helpful although it does provide the principal rationale for a great deal of the recreational activity being developed now for the retired and the aged

Fourthly another way of looking at retirement is in terms of the degree of *social isolation* that retirement imposes upon the individual For example in our society—and we certainly have been struck with this in the people with whom we have been dealing—it is perfectly clear that the occupational role and our occupations are coming to furnish each of us more and more with our major resources for social interaction for status prestige satisfaction recognition achievement, etc. Before the present degree of industrialization most of us had other auxiliary social roles that we could fall back on now to a certain extent we are ourselves becoming almost equivalent—including our personalities I might add—with our occupational role This means that retirement is not simply a loss of an activity or the loss of a skill but may mean the loss of social status

A fifth way of looking at retirement is in terms of the *loss of income* that results Financial security for the retired person is certainly of importance but it cannot make up for unsatisfactory arrangements in other areas such as family relationships social participation health social roles etc. At the present time most of the planning being done is connected with pensions and financing Other areas of planning are scarcely recognized yet or prepared for The preoccupation with money in retirement adjustment reflects the orientation of the whole society and there is a tendency for us to feel that if financial planning is complete all other things become possible We tend to feel that if people have the money they can

buy their way out of any other problems that may arise The data so far do not bear this out, and suggest that exclusive emphasis upon the importance of financial planning is a mistake While an increase in pensions is needed everywhere no amount of money can deal with many of the problems faced by the retired

A sixth meaning of retirement may be based upon the resulting change in *social status*—that is the place in a particular system which a certain individual occupies at a particular time [1] In our society the fact that an individual works gives him a certain status in his family and in other social situations Furthermore his status in the particular occupation or institution is itself an important source of satisfaction and self esteem Retirement may therefore mean not only the loss of status with respect to the occupation itself but secondarily it may (and often does) mean a loss of status in other areas of activity and participation in our society The position as head of the family may pass to one of the children or even to the wife The retirement from occupation may signal the transition from the "useful to the useless from a functioning member of a work-oriented society to the status of an unoccupied aged person

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All these ways of viewing retirement are probably relevant at various times and for particular people For our purposes however, we have found it most valuable to view the matter of retirement as an example of transition and social change In doing this we need to extend studies of transition made in respect to disaster and migration and particularly to study the natural history of the process of retirement in the same fashion as we have studied the natural history of disaster and migration [illegible]

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[1] Here [illegible] of status [illegible] of the other [illegible] society to include position in each

ment and financial circumstances depend for their significance upon the more fundamental or general problem of the availability and the taking of significant social roles

We have not found it useful for example to view the problems of adaptation to aging and retirement as dependent upon some hypothetical degree of social isolation We have been more impressed by the difficulties of getting a reliable index of social isolation that is of real psychologic significance and of the discrepancy between any objective definition of isolation and its psychologic meaning Some people seem objectively to be very isolated to have few contacts to participate little and yet from their point of view they are not isolated On the other hand people of many contacts appearing busy and active often report feelings of loneliness and isolation We have found instead that social isolation appears to depend upon the significance of the available and assumed social roles

Again we have found that the concept of activity so often used to provide the rationale behind various kinds of recreation and social program is inadequate An activity simply in and for itself has little value unless the activity has some real significance for the person The value of activity seems to depend upon its relation to a social role

What roles are available to a retired person and what ones are actually used?

First of all the individual may develop another occupational role—a second career to take the place of the first We have seen this on a number of occasions it can be a very satisfactory solution In effect however the person has not retired from work and we should attempt to discover those roles that are available and useful to the retired person

Second are the various family roles—husband parent grandparent head of the family etc Where a family role is maintained and not threatened by loss of status following retirement it is a major asset Particularly in our population which has a strong French Canadian representation we have observed the great value of various family roles for retirement in later life

Third are various member roles in social organizations formal and informal In addition to making the most of roles in sport religious or philanthropic organizations some of our pensioners have actually created significant member roles for themselves outside of a second occupation or a strong family situation

These various possible roles are by no means available to many retired people however Unable to secure employment having relied upon their previous occupation for social relations they may have done little to develop member roles in society or they may have no family to which they can turn There is no retired role as such in our society We have some

fictions about it such as the idea of fishing trips, the home in the country, the little cottage and so on But the role does not actually exist as a member role in the society Nor is there any recognized role of 'elder in our society which is a function primarily of age in years as a primary determinant of a social role Instead, the older person is expected to take roles which are customary for a younger age group in the society so that there is a tendency to see as well adapted the older person who does not show his years is just like a youngster, and so on That the adjusted old or retired individual should show his years' is ironically enough a statement that he is not adapted

We have been impressed by the fact that in the absence of other significant roles some older or retired individuals resort to an assumption of the "sick role In the presence of illness this is a legitimate social role with its own socially sanctioned patterns of expectation and response With the development of some of the normal infirmities of older age such infirmities are often used as a basis for developing a social role resembling the "sick role that for the individual bereft of other roles is better than nothing The person who assumes it has some significance at least can expect certain responses from others has a place in society and can be expected by society to do some things and not others The role can provide a rationale for little activity for diminished social participation, for dependency for being around

The assumption of the sick role in connection with aging and retirement seems much more common than is usually recognized The statement has been made, for example, that programmes for reemploying older people cannot be expected to do much toward relieving the whole range of problems faced by the aged to a large extent this is because 77 per cent of the older men who are not in the labor force feel they are not well enough to work' While it is clear that many older persons are not well we have found that statements of poor health are often rationalizations of other issues It is often an enabling factor, for example, on the part of an employer or employee to achieve retirement, it often is a way of rationalizing the disinclination to take work that is different from that for which the individual was trained or in which status would be low Most reemployment opportunities apart from self employment, involve considerable reduction in status Our data show no deleterious effect of retirement upon morbidity or mortality rates in fact there is a frequent tendency for health to improve after retirement A number of those who were in poor health at retirement have subsequently been in good health and have achieved a full time occupation

Finally in considering the question of adaptation to retirement we have been most interested in the concept of time in organizing our data More

specifically we have found it useful to consider the time perspective of the individual in relation to his retirement adaptation

Thus for example some people approach retirement with a strong future orientation—that is for ten or fifteen years before retirement they have been actively planning for the future They have been able to think about the future not only in terms of solving problems but also in terms of projecting their fantasy ahead to see what problem exists and in testing trial solutions and in preparing themselves for them Other people have been completely incapable of doing this instead they approach a problem on an *ad hoc* basis

We have been able to identify two types of *ad hoc* solutions so far One is the type of *ad hoc* solution in which the individual comes to the problem and simply responds to it responding to the nearest and most available aspect of the problem Some people do quite well on this basis and particularly in a fluid society such as ours this is often quite a successful perspective Again other people come to retirement without any planning at all but when they are faced by the situation they are able to stop for a moment diagnose the situation on an *ad hoc* basis and then project themselves into the future in terms of a series of trial solutions

We are not sure yet of the origin of these time orientations nor of their exact significance in relation to the process of adaptation Nevertheless various kinds of adaptation appear to have characteristic time perspectives

3 RETIREMENT WITH SPECIAL EMPHASIS UPON RETIREMENT PLANS

DWIGHT S SARGENT

In the limited time that each member of the panel has been allotted I am going to try to indicate some of the high spots that would be appropriate to the subject assigned to me

In 1941 there were less than a thousand pension plans in the country and less than a million individuals were covered by these plans By 1951 there were nearly twenty thousand pension plans and some ten million people covered by them In addition there were some four or five thousand profit sharing plans covering possibly three million additional people In many cases these profit sharing plans served as a substitute for a pension plan If you assume that there are some sixty three or sixty four million people now employed it appears that possibly fifty million workers today are not covered by any pension plan whatsoever—except of course for Social Security

In 1951 there were some 13 700 000 people 65 years of age and over This number it is estimated will be doubled in 15 years An analysis of

the individuals who were 65 years and older in 1954 breaks down about as follows four million were working, six million were not working and receiving a pension from some source, two million were receiving public assistance, the remaining two million were either substantially without funds and dependent upon children or relatives or were the exceptional persons who were well enough off so that they did not need to work

Another significant statistical piece of information is the following From 1910 to 1953, the number of people 1 to 17 years of age in the country increased 29 per cent The number from 18 to 64, which represents the group supporting everyone else, is up only 10 per cent, and the number of people 65 years of age and up has increased 47 per cent

A recent analysis by the National Industrial Conference Board covering 327 companies indicated that 82 per cent of the companies specified age 65 as the retirement age for both men and woman, 12½ per cent specified age 65 for men and 60 for women Approximately 4½ per cent specified retirement ages varying all the way from 60 to 75

Over the past five years, a few companies have increased the retirement age for women from 60 to 65 and from 65 to 68 or 70—generally, in each case, to the equivalent age in effect for men It is interesting that another utility in New York City has a retirement age for women of 65 We have age 60 I am sure if I proposed that they reduce their age from 65 to 60 they would be very much against this, because of the substantial increased cost of pensions that would result from such a move Many companies which have age 60 as a retirement age for woman are still disinclined to increase the retirement age and make it equivalent to that for men for reasons that appear not to exist in companies where they have age 65 and have been allowing women to work to that age for some time

An obvious conclusion certainly is that if the number of people 65 years of age and over increases markedly, something must be done to provide work possibilities or more adequate pensions We cannot afford to see a large and increasing segment of the population feel like the shoemaker's children

Six or seven years ago I heard Doctor Sumner Schlichter say at a Chicago Personnel Meeting that if employers continued to retire people at 65 the cost of pensions could go up to something like 17 per cent of payroll He also felt that a very simple way to control this cost was to let people who were able to work continue to work beyond 65 We promoted the idea in our own company and were able to send out a notice as of January 1953 that we could hold over a person year by year beyond the normal retirement age of 60 for women and 65 for men—provided a person was needed, as measured by the fact that he would have to be replaced and provided his work performance was satisfactory as measured by attendance physical

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restrictions and quality and quantity of work performed In this three year period we have actually held over only a small portion of the number of people who have come up to retirement age something in the order of one hundred people but we have secured a fair amount of information about individuals who have reached the retirement ages for men and women Our records indicate for example, that for a hundred men coming up to age 65 forty are not doing well enough in the job that they are in to cause us to want to hold them over They have either lost too much time because of illness or been limited by the doctor or just naturally slowed up There is no doubt but that possibly a third to a half of these men are physically able to do other lighter work than their regular work We have not gotten into this area yet at all as our ratings are based only on the jobs they are in at the time they arrive at age 65 Of the remaining sixty men twenty five do not want to continue at work We know that some of these simply want to quit work Others have been looking forward and have made arrangements to do some other activity after their retirement from our Company The remaining thirty five men would like very much to continue at work in the jobs they are in This analysis made after reviewing the records of about twelve hundred men indicates to us that of every one hundred men coming up to age 65 approximately thirty five individuals would be considered competent to continue working by any body s measure and if allowed to work would contribute that much more to our economy and to their own well being

During this same period we have of course developed information on absenteeism related to age For both men and women it has gone up substantially as age has increased We also have a curve showing the existence of medical limitations placed upon individuals related to age This again goes up quite sharply according to age In both of these categories the curves show the average individual s record but I have maintained that we do not consider the average individual We should be able to consider the competent individual for retention and have good evidence that the incompetent person should not be retained

We have drawn a curve showing the ratings of employees related to age The curve shows individuals who are very good or excellent The percentage increases from age 20 to about age 45 when it starts to decrease again At age 65 however 20 per cent of all the 65 year-olds have been rated very good or excellent Frankly these individuals plus some of the people rated as good are the ones that I have been interested in—trying to find ways by which they might be allowed to continue to work

We have also developed tables which for our company show the reduced pension costs for a Mechanic A for example if he is retired at age 66 instead of age 65 etc Such an individual who is allowed to work to age 68

instead of being forced to retire at age 65, will receive from both company and Social Security sources a pension totaling $32 000—instead of the approximately $40 000 which would be required if he were retired at age 65 In the case of a woman the figure is a little more startling A senior clerk for example who retires at age 68 from our company would receive from company sources and Social Security a pension totaling some $31 000—instead of the approximately $18 000 which would be required if the same woman were retired at age 60 Much of this information which I have referred to briefly is contained in some tables and charts which are available here for anyone who cares to pick one up after the meeting

My interest in this whole field was twofold first to reduce pension costs from the point of view of the company as well as Social Security and secondly by allowing individuals who are competent to continue to work, to extend the full economic value of the individual for a longer period The difficulty in getting a program of this nature accepted appears to be largely the unwillingness of many members of supervision to make the decision that A is qualified to continue taking into account all the factors and that B is not qualified It is of course, perfectly true that the cases that you review do not fall naturally and cleanly into one class or the other There are many shades of differences in work performance ratings attendance skill and ability which require judgment on the part of the supervisor and which invite a challenge by the Union if the overall judgment is not pretty solidly backed up But I am naive enough to believe that we pay supervisors because they can exercise judgment

It seems to me that if employers allow the man who is able to work to work such a man is better off himself because he continues to be a full producer and a full consumer The drain on both company pension costs and Social Sec[illegible]
marked e[illegible]
and up [illegible] [illegible]erwise have to be carried by society more—rather than less—as a dead weight group

4 SOME COMMENTS ON THE MEDICAL MANAGEMENT OF THE OLDER PERSON

DAVID SEEGAL

Informal discussions with seasoned clinicians concerning the care of the older patient cast doubt on the advisability of establishing geriatrics as an independent discipline This opinion does not invalidate the belief that the medical problems of the aged are often managed differe[illegible]
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restrictions, and quality and quantity of work performed. In this three-year period, we have actually held over only a small portion of the number of people who have come up to retirement age, something in the order of one hundred people, but we have secured a fair amount of information about individuals who have reached the retirement ages for men and women. Our records indicate, for example, that for a hundred men coming up to age 65, forty are not doing well enough in the job that they are in to cause us to want to hold them over. They have either lost too much time because of illness, or been limited by the doctor, or just naturally slowed up. There is no doubt but that possibly a third to a half of these men are physically able to do other lighter work than their regular work. We have not gotten into this area yet at all as our ratings are based only on the jobs they are in at the time they arrive at age 65. Of the remaining sixty men, twenty-five do not want to continue at work. We know that some of these simply want to quit work. Others have been looking forward and have made arrangements to do some other activity after their retirement from our Company. The remaining thirty-five men would like very much to continue at work in the jobs they are in. This analysis, made after reviewing the records of about twelve hundred men, indicates to us that of every one hundred men coming up to age 65, approximately thirty-five individuals would be considered competent to continue working by anybody's measure and, if allowed to work, would contribute that much more to our economy and to their own well being.

During this same period, we have, of course, developed information on absenteeism related to age. For both men and women, it has gone up substantially as age has increased. We also have a curve showing the existence of medical limitations placed upon individuals related to age. This again goes up quite sharply according to age. In both of these categories, the curves show the average individual's record but I have maintained that we do not consider the average individual. We should be able to consider the competent individual for retention and have good evidence that the incompetent person should not be retained.

We have drawn a curve showing the ratings of employees related to age. The curve shows individuals who are very good or excellent. The percentage increases from age 20 to about age 45, when it starts to decrease again. At age 65, however, 20 per cent of all the 65-year-olds have been rated very good or excellent. Frankly, these individuals plus some of the people rated as good, are the ones that I have been interested in—trying to find ways by which they might be allowed to continue to work.

We have also developed tables which, for our company, show the reduced pension costs for a Mechanic "A," for example, if he is retired at age 66 instead of age 65, etc. Such an individual who is allowed to work to age 68,

doctor else what useful purpose would be served by frequent calls in the many instances in which specific therapeutic measures were not available This attitude is essential in the care of the aged Its performance is more easily accomplished by accepting the principle that the physician should treat each patient the way he would wish to be treated if he were that patient in that bed at that time

Dana W Atchley in his teachings points out that the principles of medical management are essentially the same for individuals of all ages albeit the same medical problem is handled differently in different patients He uses this telling analogy The principles of driving an automobile are uniform but one drives in one manner on the New Jersey Turnpike and in another manner on a narrow winding road in the Rocky Mountains

Atchley has suggested that the total medical needs of the older patient may be better served if the thought expressed in the word appraisal be substituted for diagnosis and the word management be substituted for "treatment or cure Such an attitude would assist the physician to shift his preoccupation with cure to a fascination for management of the sick individual This is particularly important in the care of the older patient where the impact of living adds its weight to the burden of disease The elderly patient may be cured of his fever but a comprehensive history and inventory may disclose personal problems more damaging than the fever"

The modern school of restorative medicine led by Rusk and his asso ci at h

[illegible] sick patient to achieve his fullest physical and social potential This may mean such limited progressive actions as these to [illegible]

[illegible] he should be permitted to be as active as he wishes without injuring himself

The older individual in the United States does not usually enjoy the familial status and privileges accorded the oldster in the China of the recent past He may possess a social security card but he has relinquished his seat in the subway and the authority which commands the obedience of his children The elderly American of today is often preoccupied with his good recollections and his bad memory He may become a nuisance to his young associates because of his irascibility his mutterings [illegible] dentures or the [illegible] stool W B Car[illegible] the elderly in s[illegible] [illegible] activities Although the layman is

The disorders sometimes listed under the category of geriatrics are being vigorously investigated in the modern university hospital and research institute Studies of the biology and thus the aging of the individual cell and such multiple cell organisms as man are being conducted in most colleges and medical schools No useful purpose would be served by dissociating these innumerable researches from the disciplines of biology and medicine into the proposed subspecialty of geriatrics

Long term medical care of the aged in the home is often difficult to arrange to the satisfaction of the patient and the family Institutional care of the aged sick is largely provided by tax supported hospitals for the chronically ill These services are often inadequate but the trend is toward improvement in many areas particularly where an affiliation has been established between the hospital and a university Opportunities should be developed to further knowledge concerning the impact of present and changing socio-economic and socio psychologic forces upon the older individual and those members of the family unit who are perforce affected by the presence and pressures of the patient

It would appear that the needs for the physician s training in geriatrics can best be met by strengthening the university s facilities in the basic sciences and the established clinical divisions Many opportunities for demonstrating the special medical needs of the older person are available in institutions for long term illnesses since the majority of disabilities associated with chronic diseases occur in middle and late life

An expected difficulty encountered during instruction of medical students in the management of the aged patient is the retarded interest of the student in the slow changes observed in this sick group compared with the spectacular therapeutic responses often seen in younger patients with dramatic acute disorders It is only when the student comes to appreciate that the bulk of his future practice will consist of individuals often aged who harbor slowly progressive morbid processes that he is awakened to the need of enlarging his horizon as a human being and as a physician

The satisfactory management of the older patient depends upon the presence of the experienced and empathic physician The writer has drawn heavily upon the opinions of such individuals for the notions now to be presented

Although the physician is usually depicted as a healer his office might be cast in a more positive light with respect to the management of the elderly if his goal were set at assisting the patient to achieve the greatest degree of happiness under the special circumstances I remember a ward walk on a visit to Baltimore some years back In the course of the morning Dr Longcope had occasion to remark that each patient ought to feel somewhat the better for the physician s visit This was a responsibility of the

old in a special category most of what we can say is best phrased negatively What for us are the special prerogatives of the old? *not* to work *not* to pay certain taxes *not* to participate fully in on-going life—our elder States man is at best an adviser—*not* under some circumstances to get up Where others should be up and doing the really aged need not they may, if they and others accept their agedness legitimately be bedridden and dependent In this matter of dependence, we classify the very old with the very young in contrast to the adult generation but with this difference about the very young we say "Not yet about the very old we say, Not any more The young are becoming the old have been The young are getting going the old are slowing down the old can no longer learn anything new, they are coming to a stop And when we tell a person that he must slow down must take it easy must sit quietly we are not telling him that he is now at last moving into a position of dignity and strength and power that he is arriving at the high point of his life—as would be the case in China, where old age is the reward of living—rather, we are dooming that person to slow extinction we are telling him he is now and henceforth a has been.

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an ... see the climax structure of human life as rising and accelerating until it reaches a peak in what is now—in terms of life expectancy—middle age what happens thereafter is a falling off The best we can do when the bank president has been made chairman of the board is to say he has been kicked upstairs —and everyone knows this upstairs is a euphemism for down

It is also conspicuous that when—as here today—we try to create a new image of old age which will give us more constructive ways of handling the problems of aging we classify the old with those who are in some way sick or mutilated And so we speak of rehabilitating not only the paraplegic or the victim of polio or the recovered TB patient and we speak not only of rehabilitating the socially mutilated—the delinquent and the criminal—but also of rehabilitating the old Building on our existing image of the old person who is somehow down and out we seem to want to bring him back to life It looks sometimes as if what we are trying to do is to cure old age of its oldness

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... at make such attitudes as ours inevitable We can ask questions about climax structure in life—about the way in which a people visualize growth and maturity and aging we can ask questions about the special roles of the aged in relation to other people in their own

apt to have limited tolerance for the soliloquies and complaints of the older patient, the physician does not have this privilege

The principle of minimal interference is paramount in the management of the elderly The older a patient, the less his way of life should be dis turbed Destruction of an established pattern of life may result in confusion and tragedy The young amorphous personality can usually be vigorously molded without danger In contrast, the older, more rigid personality is like a crystal—easily shattered by unwise impacts

There is no specific remedy for aging G R Cameron holds the view that aging represents the vector sum of a number of morbid processes most of which take a time to develop and often a long time to reach a serious climax Cameron (as well as others) believes that many of these pathologic states begin in early life Hope lies in learning more about the beginnings of these disorders their causes and mechanisms It may not be facetious to remark that the proper approach to geriatrics is through pediatrics Charles Minot hypothesized that senescence begins at birth Montaigne put it this way Death is but an end to dying

But fortunately man has an elusive way of procrastinating with death if not with dying The physician s role in managing the elderly patient may be expressed in the following general terms a) The practices of good medicine are to be made available to him regardless of whether the disorder is acute and flagrant or chronic and indolent b) The crystallized life pat tern of the elderly patient makes serious interference perilous c) The goal of the physician is to assist the older patient to reach the highest physical and social potential regardless of the nature of the illness

5 EFFECTS OF CULTURAL ANTICIPATION AND ATTITUDES TOWARD AGING

RHODA MÉTRAUX

Most conspicuous in our American attitudes toward aging is our tend ency to avoid the whole subject Just as we have attempted to remove the visible signs of death and mourning from our homes so too we have at tempted to remove the most evident signs of aging from our images of the old The men and women who grace the advertisements for retirement insurance, the men of distinction crowned with white hair are obviously vigorous active and unwrinkled As we like to picture them, they are in the midst of life even though on perpetual vacation from real activities And the rare person who—like myself—greets with open enthusiasm the roles and possible rewards of middle age is responded to with disbelief and amusement

Secondly, when we do think of old age, when we Americans do place the

est point in old age with the expectation that it may continue to rise in later life as well In China it is not the young scholar but the old scholar who is able to achieve the greatest originality, who acts with the greatest independence and vigor there contemplation is not passive but active And if we look at the practice of traditional forms of medicine in China we can see that aside from the idea of keeping life going the main emphasis is upon the support of strength and vigor in old age Again this contrasts strongly with our own view

So a comparative view indicates most clearly that the attitudes and expectations which we—or the members of any society—have about old age about the behavior of the old as their age increases about the relations of younger and older to one another are not inevitable but within a very wide range are man made and learned as part of the total life of the society and therefore through new learning can be modified

6 PSYCHOTHERAPY OF THE AGED PERSON

JACK WEINBERG

There has in recent years been an accumulation of evidence that psychotherapy in the older age groups has been quite rewarding From the early paper by Abraham (1) to the more recent ones by Grotjahn (5) Gitelson (3) Goldfarb (4) Linden (5) Wayne (7) Weinberg (8) etc the enthusiasm for increased psychotherapeutic efforts as applied to the aging has grown However the time alloted to these prefatory remarks precludes an a le ate 1

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society, we can ask about the unique characteristics of the aged that are singled out for attention, we can ask about attitudes toward death and ideas of future life after death What do we find?

Unfortunately, few such studies have been made on a comparative basis But one may cite Simmons *Role of the Aged in Primitive Society*, in which Simmons compared the position of old people in 71 different tribes A few general points of interest come out in this study—for instance, that the old on the whole have fared worst among peoples who have lived in extreme climates, especially in very cold climates, and among those who are wanderers—wherever, in fact, resources have been limited and dependents are an inevitable burden There the old, like others who are weak or sick, have had to be abandoned In a few such societies suicide or the killing of the old has been given a special dignity, this is the good way to end life And the old have fared best in those societies where people live a settled life, where property rights are recognized or the community emphasizes sharing of resources Particularly they have fared well where the old share in the prerogatives of all adults—as in the continued use of property, in the continued exercise of power and authority—where, indeed, such things are enhanced when they are related to old age And they have fared well when the rights of adulthood are inalienable—where the king and the noble and the priest and the scholar and the parent cannot be shorn of their prerogatives because of age This, of course contrasts with our own situation aside from university degrees we have no inalienable positions And, though this may be a double-edged sword, the aged fare well in those societies where age is given unique prerogatives and is seen to have unique characteristics In many societies it is the young not the old, who may not do this may not eat that, may not speak or act independently and in an initiatory way Rather this is the right of the old In these circumstances, the old may be well off, but such sometimes are also—as witness, for instance China and in some ways France—conservative societies where the central problem is likely to be that of introducing any change smoothly into the on going stream of life

But the most important finding perhaps of comparative studies of old age and attitudes toward it, is that there are very few single regularities of behavior and belief and image that are absolutely related to it Take the whole matter of climax structure Where we see life in an upward and then downward descending curve and relate to this activity prerogative, ability to learn, and a whole gamut of ideas and images this is but one possibility In Bali with its belief in reincarnation we have rather a circle where the old and the young are close together because they are both sacred and close to heaven Or we may consider China where the child early becomes adult like there the line of living rises slowly slowly throughout life to its high

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society we can ask about the unique characteristics of the aged that are singled out for attention we can ask about attitudes toward death and ideas of future life after death What do we find?

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The outstanding characteristics of senescence which threaten emotional health are the physical decline loss of erotic values loss of supportive figures social and economic insecurity and the gradual constriction in the flexibility and plasticity of the adaptive mechanism The decrement in personal physical and emotional assets and the absence of hope (a vital ingredient for ego integration (2)) for a better tomorrow greatly endanger the adaptive capacities of the ego To master the threat of dissolution of its boundaries the ego will utilize all of its previously learned defenses and add some new ones to its repertory The major defenses employed by the ego in later life are those of regression rigidity and the exclusion of stimuli

Regressive symptoms are easily discernable phenomena and I need not elaborate upon them However few recognize in rigidity the dynamic principle of a defense We live in a highly complex and ever-changing world demanding of us constant re adaptation To master new situations requires the greatest efficiency and integration of the ego The decreased efficiency of the ego in the elderly almost always calls forth anxiety when re adjustment is necessary To avoid anxiety the aging person will cling to *automatized* and familiar patterns of behavior no matter how faulty they may be He reacts to new situations as to some danger with peevishness *irritability* and hostility Change is regarded with paranoid suspicion and fear and *the individual* will cling to behavior which has heretofore given him the *nearest* approach to mastery of his environment This is the famil iar con

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s of the psyche as set up by the ego This is particularly true of the sensory system The diminution of visual and auditory acuity in the aged are notable examples Yet there is something selective about the two *which* can be explaind only on the basis of the exclusion of some stimuli when energy *to perceive* interpret and cope with new stimuli is at a low ebb This symptom differs to my mind from that of denial For the latter presupposes something perceived and the withdrawal of cathexis from it *Not so in* the exclusion of stimuli where no original investment of energy takes place

All of these defenses are dynamic mental processes rather than fixed habit patterns with *organic* substrata and are therefore not beyond therapeutic reach The *therapeutic* goal then is first to understand the symptoms then to modify alter or work for the acceptance of some of them without resigning necessarily to *further* deterioration

Lastly it is the therapeutic function of the psychiatrist to manipulate the environment in which the older person lives This may range *from the* education of the family friends and those who are entrusted with the care

the part of the objects There is nothing left but new methods of adaptation some patently pathologic defense maneuvers or the turning of these liberated energies inwardly *What emerges is a seeming regression to a narcissistic state* (To my mind this is technically not a regression The organism does not withdraw its cathexis it is forced by the environment to push *it back onto itself*)

To ameliorate the arising pathology, the psychiatrist s role is a triple one The first is his relationship with the patient In 1951 I stated it as follows

*From time immemorial man has struggled with the irrational forces under*lying emotional disturbances Everything conceivable has been tried by those who have been called upon to treat human beings Psychiatrists have *gone a long way from the days when through incantation and prayer, man* tried to placate and drive out the evil spirits We have attempted brain surgery and shock treatment long term psychotherapy short term therapy, *individual psychotherapy group therapy*, various drugs *heat and cold fire* and ice music sociodrama hydrotherapy, occupational and recreational therapy total push to total regression all have been tried and to all have *been ascribed healing powers by those who promulgate their favorite* means The confusion resulting from all of the claims becomes no confusion when one realizes that all of the above therapies have a common denominator *The common denominator is of course the therapist and the patient* the interpersonal relationship between them or as the psychoanalyst refers to it the transference phenomenon

For no matter what the treatment may be—and there are of course valid and intrinsic values in all of the above named methods—it is nonetheless the awareness on the part of the patient that in the therapist he has an individual *who is ready to understand willing to give and to help* which is beneficial and therapeutic

What I said then holds true today and certainly coincides with the *thinking and experience of the clinicians mentioned previously* All recognize the enormous importance of the relationship and the role played by the psychiatrist The need is for an enthusiastic optimistic approach which *is genuine* and active participation in the relationship which depends as much on its quantitative aspects as it does on the evaluation of its quality The psychiatrist working with the aged must free himself of his feelings of being bound by formalistic approaches to therapy He must be willing to venture out and try out modifications of traditional techniques Certainly the psychoanalytically trained psychiatrists who have reported on their therapeutic successes with the aging cited their more active role were ready to do away with the couch and allow themselves to enter more freely into a relationship with the patient

Secondly the psychiatrist must be aware of the nature of the pathology

Today we have a large attending staff comprised of internists and representatives of the various specialty groups Our total population today consists of 371 at Central House 376 at Kingsbridge House 166 in our Apartment Projects and 93 on our Extra Mural Care Program or more than 1000 men and women An active research program is carried on in internal medicine neurology and psychiatry ophthalmology and clinical psychology We take great satisfaction in having stimulated other homes for the aged to improve the quality of medical care given to their residents

Long before the word rehabilitation had acquired an upper-case initial letter we had evolved a program of physical and mental hygiene designed to prevent infections accidents and mental breakdowns as far as possible particularly emphasizing the need for rebuilding the confidence and self respect of individuals to whom admission to a home for the aged constituted a complete collapse of all their hopes and aspirations

The word rehabilitation is much misused and misunderstood Speakers often fail to specify whether they are discussing physical mental social or economic rehabilitation The unfortunate association of the word with physical medicine tends to limit its use to physical means of therapy Actually rehabilitation is both a theoretical concept or attitude and a method of therapy I h d

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one of Dr Rusk s disciples and has made a great contribution to our handling of hemiplegia chronic arthritis hip fractures and other common disorders of the aged Only two days ago we showed for the first time a medical documentary film entitled Still Going Places which is devoted to the active management of disability in the aged This film was made possible by a grant from Pfizer Laboratories division of Charles Pfizer and Company and is available for medical audiences through this pharmaceutic house The subtitle of this film The Active Management of Disability in the Aged is a good definition for our kind of rehabilitation In our institution we think of rehabilitation as a total job aimed at the whole human being In fact we pride ourselves on a truly patient centered program In achieving such total rehabilitation the cooperation of every member of the institution s personnel

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of the aged as to the needs of the patient and the meaning of the symptoms, to a dogged gnawing at the conscience of society for a better emotional climate for our aging population.

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7. REHABILITATION OF THE AGED

FREDERIC D. ZEMAN

As an exponent of the far flung specialty known as internal medicine, I have had experience in the care of the aged in general hospitals and in institutions for the aged, as well as in private practice. Over thirty years ago, I took over the medical management of the Home for Aged and Infirm Hebrews of New York City, at that time a pleasant boarding house for some 100 men and women over 60 years of age. I soon became aware that the application of standards of medical care such as were then current in general hospitals to the problems of my elderly charges would prove worth while. Accordingly, periodic physical examinations were instituted. Improved nursing care, a social service department, occupational therapy, physiotherapy, diagnostic laboratories and diagnostic x-ray equipment were in time installed. With the provision of a new building, it became possible to provide a pathology laboratory with opportunities for post mortem examination. In recent years, departments of neuropsychiatry, organized recreation, and rehabilitation and physical therapy have been added. Today, the Home has become an intermediate medical facility, approved by the Joint Commission on Hospital Accreditation and filling a gap in the over all community medical picture. It takes care of older people, on a long term basis, according to their medical and social needs. Close cooperation with other medical facilities is our practice, since the Home does not provide specialized services such as surgery or deep x-ray therapy

can learn from the psychiatrist just as the psychiatrist can learn from him Psychophysiologic reactions are most intimately and delicately balanced in the aged.

In conclusion, I would stress again the concept of rehabilitation of the aged as a total effort in which the internist, the neuropsychiatrist, the physiotherapist the nurse the social worker must all play an important part. The basic principles stressed have emphasized the physician's atti tude precise diagnosis caution in drug therapy, more courageous surgical approaches more rehabilitation and physical medicine, and more psychotherapy

In the words of Sir James Crichton Browne, "There is no short cut to longevity, to achieve it is the work of a lifetime"

DISCUSSION

CHAIRMAN CAMERON Thank you Dr Zeman I think the panel is to be congratulated in getting through so expeditiously I am now going to ask the members of the Commission if they have any questions they would like to put to the panel

PRESIDENT MOORE I should like to address a question to Dr Meyer To what extent if at all are acute delirium confusions or anxieties in elderly patients correctable by means of tranquilizing drugs? If these drugs are successful in the control of the acute situation how long should they be continued to minimize relapse? What are the drugs of choice and what are their effects?

DR. MEYER I would say that the acute reactions of delirium are easily reversible and as a general statement, this is true—provided that you add to that the reversibility of the acute physiologic imbalance that is contributing to the disturbance

Drugs in my opinion are only a temporary expedient in dealing with acute reactions while our experience has been limited we have come to be more and more conservative about the use of tranquilizing drugs particularly reserpine When they are given blood levels are obtained which produce the desired effect but the drug is retained in the body for a period of at least three or four or five days In the long term maintenance of acutely disturbed elderly people one runs the risk of depriving the patient of what I would call the antishock defenses such as tachycardia the hypertensive response and sweating so that if he comes up against an acute surgical emergency [illegible]

then den[illegible]

We [illegible]

with th[illegible]

over th[illegible]

[illegible] meanwhile trying to ascertain the multiple factors that might come into the particular disturbance that we are dealing with

CHAIRMAN CAMERON I am going to ask Mr Sargent this question He mentioned that quite a high percentage of workers do not want to continue after the retirement age I would like to ask him does he find that motivation to continue working is related to any of the following factors 1) the job category 2) the social class 3) the cultural sub group or 4) the individual traits?

MR. SARGENT I would say that a third of our people want to continue There are 40

reputation whose orders are carried out by a capable resident staff gives our residents basic health security

Our psychiatrists have been successful in developing methods of psychotherapy suitable for use in elderly patients We are engaged in experimenting with small sections for disturbed individuals and find that within the framework of our organization we can take care of many such elderly individuals without the need for transferring them to state hospitals Naturally the use of tranquillizing drugs such as Thorazine and Serpasil has been of the greatest value

Elsewhere I have emphasized certain basic principles in the therapy of older individuals which may be briefly stated here as the basis of a total effort at rehabilitation in private practice

1 Diagnostic precision is the basis of all therapy "There are no diseases peculiar to old age and very few from which it is exempt" (Worcester) It is necessary to detect all pathologic lesions present in a given individual but it is also important to estimate the functional capacity since there is often a great difference between the two The wise practitioner will also appraise the social situation as to family relationships housing economic status and their relation to community organizations He will avail himself of the expert assistance of trained social workers and visiting nurse service and will apply to his own work the lessons learned from the success of team approach in institutional practice

2 The physician must be convinced that his efforts for the old are in the highest traditions of our profession and that working among the old will take his best efforts A genuine liking for old people is a great asset

3 Knowing the limitations of the aged organism the physician must be satisfied with limited goals Palliation is in itself a worthy objective

4 Overdosage with drugs of all kinds which should be avoided at all ages must be even more carefully avoided with the old Observations on the efficacy of the drug must be rigidly controlled

5 The assistance of specialists in rehabilitation and physical medicine must be utilized and their teachings always kept in mind The patients must be kept in motion They must be taught to help themselves No effort must be overlooked in teaching the patients how to get to the toilet by themselves

6 The contributions of modern surgery in bringing benefits to the old are expanding rapidly New operative techniques new methods of electrolyte control in preserving fluid balance the use of transfusions light anesthesia all tend to reduce operative risk and operative mortality The physician must not wait too long for elective operations

7 The physician must realize that everything he does is psychotherapy The old intuitive methods are now passé The physician caring for the old

to is not necessarily a very exact evaluation of the situation In some, we have found that health is most frequently used as an enabling factor

CHAIRMAN CAMERON Well I thought I could rely on Dr Tyhurst to disagree May I ask Dr Romano to say a word on this point?

DR ROMANO As a matter of fact I wanted to ask three questions I don't think any of them has to do directly with this point The first question I would like to direct to Doctors Meyer and Weinberg As I understand it in the short time they had to present their data both of them pointed to the fact that there were many similarities in the various crises experienced by older people as compared with people of other age groups I just wondered whether they would consider this matter now that there is a renewed interest in more precise studies of cognition—those in the fields of perception, thought learning and memory—perhaps one day when these studies are completed we will obtain clues and understanding and skills which will better prepare us to deal with some of the problems of the aged than we have now

We all know that with the impact of psychoanalytic psychology in this century we have devoted a tremendous amount of attention to the conative and affective aspects of motivation and behavior but now that cognitive studies are being done in a much more sophisticated manner than had been done before this century we may be able to learn something more of the way in which the mind works at certain periods

The second question I would also like to direct to the clinicians Doctors Meyer, Tyhurst, Seegal and Weinberg It has been mentioned here a number of times that the patient is the unit of study but as a matter of fact a number of people feel that this is not so—that actually the unit of study is the family rather than the patient Would they comment for a moment on the ... of
education in this country of direc ...
Campbell's definition of some ye ...
sickest member and that one certainly cannot obtain a complete or even intelligent understanding of the behavior of people particularly the aged without some reasonable understanding of the social dynamic steady state of the family of which the patient is a member?

My third question I would like to direct to Dr Metraux I was very much interested in her statement of the cultural stereotype in terms of anticipation in attitude of the aged in our society I would like to ask her are there media now extant in our culture such as television news programs and occasional drama which may bring about some change from the existing stereotype of the nubile young woman and the vigorous young male? Isn't it true that for the first time in our generation the human face is being seen by a great number of people as it actually is rather than through the stylized version of the American movie industry and the magazine pictures? Is it true now that we see young and old as they are with the lines of care and worry and joy and pleasure and anger on their faces rather than the samples which the movies have given us for some time?

CHAIRMAN CAMERON Do we have the answer to the first question?

DR MEYER I agree very much with what Dr Romano said when he underscored the potential usefulness of the current studies on perception thought process learning and memory Particularly I think the matter of the studies on the organization of perception are relevant to the problems of the aged person who is sick and also disturbed mentally

per cent whom we don't want to keep I don t know frankly, how many of them want to stay

I think, by and large the main reason for wishing to continue is to keep on the pay roll to earn full pay instead of having to get along with $180 or $190 a month

We have done quite a bit of work in trying to get people to think about retirement and plan for it but too many people haven t thought about it and when it comes to them they don t know what they are going to do and they feel lost for a period I think after two years they are very happy

Now, what was the second one—the social concept?

CHAIRMAN CAMERON Social category or class—the social stratum from which he comes

MR SARGENT No I would say that the main reason why most of the people wish to stay on is simply an economic one

CHAIRMAN CAMERON I wonder if there is any disagreement—and let s hope there is—between Dr Tyhurst and Mr Sargent about retirement? Do you care to debate between yourselves?

DR TYHURST I would like to disagree in principle anyway Mr Chairman Concerning voluntary retirement we found that statements of the company were quite unreliable that in fact the voluntary applications so called for retirement were false probably in about 75 per cent of the cases that this is what often amounts to the engineering of consent Supervisors often say to the employees You know you re due to retire in a *year or so The employee says Oh yes and then hopes it is going to be forgotten* But six months later something more is said about it eventually some statement is made about health or something like that Then the employee realizes that he is going to have to go and is not going to be able to stay on and under those circumstances signs the application form voluntarily

In the group that we are studying at least we have found when we have gone to the person himself—actually gone into the situation he would much have preferred to stay at work

MR SARGENT Just to keep the argument going we retire on the order of 400 people a year that is retire them for disability We push them out There is nothing voluntary *about it If they are sick we decide they can t work and they don t get back to the job* at all They go out for disability We have an early option whereby a man can retire if he wishes to when he gets enough age and service We have probably four applications a year for early option Of course the money is reduced somewhat But the ones I am talking about the men who come to retirement at age 65 we have talked to them and we ve got the company records on them As for the disabilities sure they would like to stay on but we push them out because they are not pulling their weight in the boat But there is very little of the early voluntary retirement

DR TYHURST I might say that the reasons for retirement are not only the problem of health I have identified a lot of other reasons such as hostility between employee and supervisor *or* reasons that are quite irrational in many instances—problems of emotion changing the job obsolescent job and so on Health and the failure of the individual to actually work on the job are by no means the most important Very frequently we also find that the statement that the individual is not working as well as he used

What we are faced with is that individuals come in to us with a variety of disorders They are patched up in one way or another and they are able to get around Some can earn a living They may have a pension, but they cannot live on that pension They may be recipients of a wide variety of relief, but not quite enough to meet the urban challenge to their economic safety

We are faced with the fact that we know very little about how to handle a situation in which a man has twelve children scattered around New York and in the countryside, and none of those children can look after him or have any desire to do so

I listened to Miss Fanny Hurst and a sociologist on television not very long ago, and Miss Hurst felt that any family that refused to take an oldster into that family was, in effect, participating in a deep tragedy to society On the other hand, I am acquainted with individuals who take the position that an elderly individual who has not quite adapted himself to this pressing civilization can not only ruin his own life but can ruin the lives of three generations

That is our dilemma. In a hospital, we are not worried about Serpasil particularly; we are not worried about aspirin we are not worried about prostatectomies Those things are quite simple Our problems are this enormous mass of individuals who have been put together again and who can go to ball games, or who might make a limited income. But the family unit, as it existed at the turn of the century, with which I was acquainted does just not exist in this urban population So I would say to Dr Romano I love that family unit, but it just does not exist in a quantitatively sufficient way to look after the large number of old people that we have with us

Dr. Romano I think my point was not necessarily that the patient should be returned to the family unit, but, rather, that the perception of the patient should be not that of a social isolate and an understanding of his behavior is dependent on knowledge of what the family unit has been and what separation from that unit means, to him and to them

Dr Weinberg Mr Chairman, having sat on the Committee on the Family in the Group for Advancement of Psychiatry for the past three years I can be most humble in terms of the family and talking about it.

Dr Romano asks an enormously important question Our understanding as psychiatrists *of the* dynamics and the interactions that occur in what is known as the family, and the implications of illness of one member of the family on the family unit, and vice versa *is very imperfect* We don t even know the anatomy of the family any more, whether it is the extended family grouping that Dr Seegal spoke about or the nuclear unit *of husband* wife and children We know so little, actually, of the dynamics and the interactions that occur in a family unit

We have been trying to formulate methods of analysis of the family *per se*—that is, the family *group*—*in order to* be able to understand how much this family unit is responsible for the well being or the ill health of the individual, and what movements into and out of *the family* unit will do both to its individual components and to the family as a *whole I can* say this much, that we all, of course are, therapeutically speaking, utilizing *the family, certainly* As an example, an 80 year old woman, who came down with a *severe memory defect*, who has been calling upon her family members to be with her at all times and has asked that old family retainers return to the fold, went into a panic *every time* some member of the family or some individual with whom she had been interacting *previously* was not about These panics became temper tantrums and outbursts and the *family* was unable to deal with them

There is the question for instance of whether distortions at the level of the sense perception themselves can be affected by anxiety as well as by organic impairment This is a real issue which is debated pro and con We are familiar of course with the grosser manifestations of perceptual disturbance in the hysteric patient where disturbance of vision 'gun barrel vision blindness disturbances of sensation and of anesthesias and paresthesias are also accompanied by impairment of motor function

The question of the minor degrees of these impairments of the perceptual process is so particularly important it seems to me because it is just the structuring of a familiar world that is the reassurance and the antidote to the internal threat which is a combination of the realistic shock let s say of the sudden onset of physical symptoms and it is also the perception and the anticipation of further perception of impairment of adaptive response Investigation in this area will be particularly helpful in furthering our knowledge not only of disturbed elderly people but of all psychologic disturbances

We are already familiar of course with the fact that we try to order or structure the external environment of the acutely disturbed elderly person We keep lights in the room at night so that the shadows do not enhance perceptual distortion We know the value of the special nurse We know the value of a familiar relative who can sometimes bring so it seems a patient out of a very acute delirious reaction because of familiarity alone when a nurse or a doctor or someone who is not familiar cannot do it

The problem of the patient in the environment where he is acutely disturbed can be further investigated not only by the experimental techniques involved in perceptual experiments but also by the clinical observations of the psychiatrist himself once he is alert to the need for close study of the perceptual distortions and their changes in the acutely disturbed patient

I might mention the study by Drs I and and Weinstein who have been interested in this problem in which the bandaging preoperatively of the eyes of the patients who were undergoing cataract operation and the postoperative disturbances were correlated with electroencephalographic changes This particular study is a model of the unity of clinical and observational data with the increased interest in the perceptual distortions and their role in acutely disturbed behavior

Chairman Cameron Thank you The second question as you may remember was addressed to four people I will ask Dr Seegal to lead off because I know that Dr Seegal has been thinking about undergraduate curriculum teaching and so on It is the matter *of the family unit rather than the individual I think*

Dr Seegal May I handle that question in three very small parts? First may I read a sentence from my prepared statement which I consider the major area of attack as I see it as a family physician Opportunities should be developed to further knowledge concerning the impact of present and changing socio economic and socio psychologic forces upon the older individual and those members of the family unit who are perforce affected by the presence and pressures of the patient

The second point I was not born in a log cabin but I have lived in a small town and my memory of it is this that when there were older members of the family unit who were disabled is was the cultural attitude to look after your own You just couldn t exist in such a community if you didn t look after your own people

Part three of my answer is this I now work in a hospital in which Dr Rusk has considerable interest We estimate that in this hospital for the care of long term illness there are 1500 patients Half of them could be discharged tomorrow if they had a family unit to return to

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We are faced with the fact that we know very little about how to handle a situation in which a man has twelve children, scattered around New York and in the countryside and none of those children can look after him or have any desire to do so

I listened to Miss Fanny Hurst and a sociologist on television not very long ago and Miss Hurst felt that any family that refused to take an oldster into that family was, in effect participating in a deep tragedy to society. On the other hand, I am acquainted with individuals who take the position that an elderly individual who has not quite adapted himself to this pressing civilization can not only ruin his own life but can ruin the lives of three generations

That is our dilemma In a hospital, we are not worried about Serpasil particularly, we are not worried about aspirin, we are not worried about prostatectomies. Those things are quite simple Our problems are this enormous mass of individuals who have been put together again and who can go to ball games, or who might make a limited income But the family unit, as it existed at the turn of the century, with which I was acquainted does just not exist in this urban population So I would say to Dr Romano I love that family unit, but it just does not exist in a quantitatively sufficient way to look after the large number of old people that we have with us

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[illegible]

vice versa [illegible] of one member of the family on the family [illegible]

[illegible]

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It was not until I was able to explain to the family that this aged individual with memory defects was utilizing the family as an extension of her memory when she was able to when she had a vacuum about something to point and say Now who was it? and the family was able to supply the name—it was only through the family's understanding that they were supplying her with some external memory, if you will that the entire situation became relaxed in that particular unit

CHAIRMAN CAMERON Are there any other people who want to answer that No 2 question? *If not I will go on to No 3 which was addressed as you may remember to Dr* Metraux Do you remember the question?

DR METRAUX Yes It was whether there were any media now for obtaining an image of what a person really looks like and it was suggested that possibly television gives us a more accurate image of the individual at any age

As a matter of fact I think that bit of it is quite simply answered if anyone has ever seen one of his friends on television or has seen him when he has just come off television It is a somewhat different use of makeup and is rather extreme Again it tends to highlight the contours of the face rather than the discriminating lines in the face etc But I think that there is something else going on which perhaps is giving us a more realistic view of the place of the aged among others in our population and that is something that has been repeated here a number of times the necessity for seeing the *elderly person as part of the on going stream of life Again and again the speakers here* have brought up that point It brings us back to give a place to and so on As I said earlier this is one of the devices that is used in many societies for protecting the abilities and strengths of the aging individual

We are also doing a number of other things along those lines tied in with that—for instance providing to a certain extent housing for elderly people or rather elderly people are picking up something which was essentially provided for the young If you look at albums and so on you will see that it is not only the very young who are getting very modern new houses but quite often it is the parents whose children are married and gone away who are *living in small modern housing and in that way they are both* physically and in terms of the image reintegrated or continually integrated into on going life I think one might find a number of areas where that is true

On the point of the family I think there is a complication for Americans We do believe in a two generation family in which the younger ones are always moving out Adulthood for all of them is dependent on independence so that we have a particular problem of what to do with the older person who if he stays with his children is deprived to a certain extent of adulthood or the children are deprived with the further complication that in American society we have people from many different cultures and who to some extent retain in their attitudes towards *old* age what they learned as small children from their grandparents perhaps who came from other countries with other expectations of what old age could be or was Therefore there is no simple image that we can work with in terms of the family

CHAIRMAN CAMERON I would like to ask another question of Dr Metraux that is it ... to clear that something is going on The mere fact that we are here today is one

you to pick up your crystal ball and look ... to it ...
great things of people who are in disciplines other than our own and so I am going to

ask you) do you see any traits or trends or characteristics of the North American culture which would allow one to foretell at least in general terms what one should anticipate might be the position of the older person in the family in the community, say, some couple of decades from now?

DR METRAUX That does need a crystal ball doesn't it? Well I think in looking at it, one of the things we can build on is the whole sense of fluidity with which we are continually working in our society so that here is a real point of contrast if we are considering modern problems of aging in Europe say or in China today as against the United States that probably we can look to a larger number of kinds of influences and a fairly large number of ways in which elderly people can find places where they belong and where they will have a kind of dignity and meaningfulness that will make them as I said part of this on going

I would say that that is the chief thing I would look to If you look at our general feeling that there is no single solution to a problem as we do feel it seems to me we should work toward—and we probably would achieve it whether or not we work toward it a great variety

There are experiments going on now in new education of elderly people in new kinds of jobs in new relationships to the family where grandparents are now not the honored baby-sitters but are the honored guest baby sitters in some family This is a very small point but a new view and I think it is the development of many alternatives that we must face and prepare for

CHAIRMAN CAMERON Thank you I would like to say that I have a number of questions here from members of the audience May I ask if the Commission has other questions to put?

DR MALAMUD I would like to address this question primarily to Dr Tyhurst in relation to his remarks on retirement although the question I think is also relevant to what Mr Sargent said and also to some extent to what Dr Meyer said because I consider retirement as perhaps one of the most important examples of so called catastrophic situations that the old person has to deal with

I should like to ask them to what extent do they consider the following factors as important in reducing pathologic effects on the retired person first the nature of the job in terms of it being time bound secondly to what extent restrictions of interest to one particular job on the part of the retiring person—a complete investment of all one's emotional interests in one job in particular and therefore having difficulty in shifting and as a corollary to that one to what extent the personality of the retiring person is related to this or bears importance to it namely the rigid person the first type of personality who has difficulty in making transitions even before the feeling of senescence? And finally the attitude of society in its willingness to take cognizance of what I alluded to yesterday in terms of the possibility of positive assets that come with age rather than to restrict ourselves to emphasize only the deficits that come with age

Last night, in a private conversation Dr Gerard rather challenged me asking me to give him examples of what types of assets I considered may come with age I was thinking at the time of [illegible] not mistaken [illegible] ... innie Mack who if I am [illegible] time [illegible] ... kind of job he was cer[illegible] in the [illegible] ... would have been a pre[illegible] years that he [illegible] ... as a baseball player [illegible] yet over the period of [illegible] he had accumulated certain experiences which

have been brought into play as assets that he probably never would have had before namely an understanding of the game Certainly I think he is known much better for his ability to manage the Athletics than he was as a catcher

If I may be allowed to take a jump both across the years and across the type of occupation I would like to remind you that when Plato wrote one of his most famous works—I don t remember exactly what age he was—he must have been between 60 and 70 He probably would never have been able to do the job that he did had he not had the *experience of his three failures in Syracuse which certainly gave him a much better* appreciation of the development of a perfect state and even in that one one may ask whether Futhyphro is a perfect state But certainly it gave him the ability to write what must be considered his greatest work

DR TYHURST The areas mentioned were job personality factors and the willingness of society to recognize positive assets

First as to the nature of the job it is certainly important in terms of retirement in the sense particularly that the higher the person gets in terms of position the more difficult it is for him to find after retirement any situation in which he can use his management skills in fact there is often a far greater difficulty and thus again is somewhat contrary to what I understood before we started this research for the person who has gotten to a supervisory job to find something to do afterwards or some equal occupation unless the person has some skills part of which can find some application subsequently Yes many of the jobs do get obsolete and this is often the basis for retirement

Restrictions of interest in particular jobs are the same problem but again this is increasing feature of people coming to retirement now because all of us are characterized not by a wide range of interests but by an occupationally bound range of interests and I think that this makes it extremely difficult for people who are not professionals or otherwise to be able to continue to maintain these interests subsequently But these are not so terribly important because I think that this depends tremendously upon the attitude of the particular individual—which takes me to the next point that is we have not been impressed by the value of the idea of rigidity in old age

Rigidity is not a feature of personality so much as it is of a situation that a person finds himself in together with his personality I would much rather see if there are such things some objective indices of rigidity that can be separated in the social situation in which the rigidity is measured If you take an old person and put him up against the situation of retirement and then say Well he doesn t adapt right way therefore he is rigid that is taking quite a step It may mean that the range of alternatives open to him under the circumstances is extremely narrow compared to the situation which a younger person may be in under the same circumstances

In brief we have found the whole concept of rigidity quite useless although we were very enthusiastic when we started out with this idea as probably being the main feature by which we would be able to investigate the personalities of the aged

The thing that we have found useful however is a habitual mode of action so to speak in which the individual projects himself into the future in fantasy for one of two reasons either to try to discover problems that he may have to meet even ten or fifteen years in the future or not looking particularly for problems but meeting problems He looks ahead and tries out trial solutions

These two features seem to be much more important than anything having to do with rigidity Rigidity seems to be so much a product of a social definition situation that as a personality feature it has not been useful

Finally with respect to the willingness of society to recognize positive assets we have

been struck very much by the fact that most of the evaluations made of aged or older people at work have been made by people much younger than themselves and that in most of the research published the evaluations of the abilities and assets of the older person were being made by people on the average at least fifteen to twenty years younger We thought this was quite important Under these circumstances it seems that the willingness of society to recognize positive assets depends upon who is naming the assets

CHAIRMAN CAMERON Dr Ross do you have a question?

DR. ROSS Yes I have two questions Bearing in mind that the topic of this panel discussion is "The Physician s Contribution to the Role of the Older Person in Society" the first would be to Dr Metraux as to how much the pattern of saying that only if a person is ready and willing and does leave his family is he showing maturity—how much does this play a part in the present two generation family which we repeatedly describe as the American pattern?—of course not in her way of saying it but in many situations with an overtone of accusation

My second question must be directed to Dr Cameron because it goes Dr Romano s one better and has five people as its object Throughout this discussion we have had (except for Dr Weinberg s saying that the psychoanalyst must forgo the *formalized* approach in order to treat the older person) no reference to the attitude of the physician toward older people and what part this plays in the efficacy of both general treatment and rehabilitation as well as the part it plays in community attitudes towards older people

CHAIRMAN CAMERON Dr Metraux would you care to aswer the first question?

DR. METRAUX That is something of a chicken and egg problem As long as we link adulthood and independence to willingness to set up a new family just so long are we likely to have a great deal of emphasis upon the importance of the two-generation family

The real question I suppose is whether there are other kinds of families in the world that do protect the adulthood of two or three or four generations who may be living in them and the answer of course is "Yes

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CHAIRMAN CAMERON
know if
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living sh ... uttering—

DR ROSS Oh no!

CHAIRMAN CAMERON Will you restate it?

DR. ROSS I really didn t communicate did I? My point was in this discussion we have

have been brought into play as assets that he probably never would have had before, namely, an understanding of the game Certainly, I think, he is known much better for his ability to manage the Athletics than he was as a catcher

If I may be allowed to take a jump both across the years and across the type of occupation, I would like to remind you that when Plato wrote one of his most famous works—I don't remember exactly what age he was—*he must have been between 60 and 70 He* probably would never have been able to do the job that he did had he not had the experience of his three failures in Syracuse, which certainly gave him a much better appreciation of the development of a perfect state, and, even in that one, one may ask *whether Euthyphro is a perfect state But, certainly, it gave him the ability to write* what must be considered his greatest work

DR TYHURST The areas mentioned were job, personality factors, and the willingness *of society to recognize positive assets*

First, as to the nature of the job, it is certainly important in terms of retirement, in the sense, particularly, that the higher the person gets in terms of position, the more difficult it is for him to find, after retirement, any situation in which he can use his *management skills, in fact, there is often a far greater difficulty, and thus, again, is some*what contrary to what I understood before we started this research, for the person who has gotten to a supervisory job to find something to do afterwards, or some equal occupation, unless the person has some skills, part of which can find some application sub*sequently Yes, many of the jobs do get obsolete, and this is often the basis for retirement*

Restrictions of interest in particular jobs are the same problem, but, again, this is increasing feature of people coming to retirement now, because all of us are characterized not by a wide range of interests but by an occupationally bound range of interests, and *I think that this makes it extremely difficult for people who are not professionals or* otherwise to be able to continue to maintain these interests subsequently But these are not so terribly important because I think that this depends tremendously upon the attitude of the particular individual—which takes me to the next point, that is, we have not been *impressed by the value of the idea of rigidity in old age*

Rigidity is not a feature of personality so much as it is of a situation that a person finds himself in together with his personality I would much rather see, if there are such things, some objective indices of rigidity that can be separated in the social situation *in which the rigidity is measured If you take an old person and put him up against the* situation of retirement and then say, "Well, he doesn't adapt right way, therefore he is rigid," that is taking quite a step It may mean that the range of alternatives open to him under the circumstances is extremely narrow compared to the situation which a younger person may *be in under the same circumstances*

In brief, we have found the whole concept of rigidity quite useless although we were very enthusiastic when we started out with this idea as probably being the main feature by which we would be able to investigate the personalities of the aged

The thing that we have *found useful however is a habitual mode of action*, so to speak, in which the individual projects himself into the future, in fantasy, for one of two reasons either, to try to discover problems that he may have to meet even ten or fifteen years in the future, or, not looking particularly for problems but meeting problems He looks ahead *and tries* out trial solutions

[illegible] seem to be much more important than anything having to do [illegible] much a product of a social definition situation that [illegible] useful [illegible] ness of society to recognize positive assets, we have

been struck very much by the fact that most of the evaluations made of aged or older people at work have been made by people much younger than themselves and that in most of the research published the evaluations of the abilities and assets of the older person were being made by people on the average at least fifteen to twenty years younger He thought this was quite important Under these circumstances it seems that the willingness of society to recognize positive assets depends upon who is naming the assets

CHAIRMAN CAMERON Dr Ross do you have a question?

DR. ROSS Yes I have two questions Bearing in mind that the topic of this panel discussion is The Physician's Contribution to the Role of the Older Person in Society" the first would be to Dr Metraux as to how much the pattern of saying that only if a person is ready and willing and does leave his family is he showing maturity—how much does this play a part in the present two generation family which we repeatedly describe as the American pattern?—of course not in her way of saying it but in many situations with an overtone of accusation

My second question must be directed to Dr Cameron because it goes Dr Romano's one better and has five people as its object Throughout this discussion we have had (except for Dr Weinberg's saying that the psychoanalyst must forgo the formalized approach in order to treat the older person) no reference to the attitude of the physician toward older people and what part this plays in the efficacy of both general treatment and rehabilitation as well as the part it plays in community attitudes towards older people

CHAIRMAN CAMERON Dr Metraux would you care to aswer the first question?

DR METRAUX That is something of a chicken and egg problem As long as we link adulthood and independence to willingness to set up a new family just so long are we likely to have a great deal of emphasis upon the importance of the two-generation family

The real question I suppose is whether there are other kinds of families in the world that do protect the adulthood of two or three or four generations who may be living in them and the answer of course is Yes

But what tends to happen if one looks for example at the traditional Chinese family is that the younger adult members develop a pattern of responsiveness rather than a pattern of initiating new action which again gets tied into a lot of other things in life so that we tie our independence adulthood initiatory behavior etc and we tend to come around again to the two generation family But it is not an inevitable conclusion You can reset your thought as it were and the things that you want to emphasize

CHAIRMAN CAMERON I am going to try this question on Dr Seegal if I may I don't know if I have it quite clearly in my mind Perhaps Dr Ross you will correct me if I haven't It is a two-headed question as I gather it The first is what general advice as to living should the physician give to the man or woman entering—

DR ROSS Oh no!

CHAIRMAN CAMERON Will you restate it?

DR ROSS I really didn't communicate did I? My point was in this discussion we have

had no reference to *the physician's attitude toward older people* as a basic component to how effective he is in his therapy, in his rehabilitating effort and in his effect on community attitudes toward elderly people We have talked entirely about the older people and how others feel toward them I am talking about the physician himself and his attitude toward aging and those who have experienced it

Dr Seegal You are raising the question of the education of Henry Adams and the education of the physician Some of us who spend our lives with medical students know that they have to make many of the same mistakes that we have made I think that enlightened attitudes with regard to what a doctor ought to think about and his reactions to patients are becoming apparent on the horizon but just because an individual is a physician does not necessarily mean that he is a mature human being He has to suffer he has to undergo experiences which help to facilitate maturation No type of education that we know of can squeeze all the wisdom into a medical student in the period of four years

A good example of that is when a medical student sees patients with diseases that he *thinks will not challenge his integrity they are just something that occurs in somebody* else But when he sees a patient of his own age on the ward with tuberculosis or an early cardiac infarct he is very much easier to convince I think we all have gone through that experience Until I had a frank shaking chill I was a very poor doctor with respect to looking after patients with frank shaking chills I must have been called a hundred times to see such patients and I moved in a typical slow fashion towards the bedside But once having gotten a shaking chill I used to reach the bedside of that patient before the patient finished half his paroxysm I think therefore the notion that because an individual is a physician he is really a total human being is fallacious Doctors are no different from other people in that respect

You have touched on the entire question of the selection of human beings the medical school attitudes and types of education experiments etc Now we have had an experience for twenty years of the following order—and this is an experiment which I can talk about When I went to medical school there were several opportunities to look after patients in outlying institutions with so called chronic diseases Any member of my class who did that or any member of my class who went into psychiatry at that time was looked upon as a secondary citizen Those were the facts Today happily things have changed

With respect to chronic diseases most students feel or used to feel that things weren't dramatic enough They wanted to see a patient coming in with a temperature of 108 and cured *the next day or an aneurysm just ready to burst If it took 18 hours it* really was too long to wait Today students realize by virtue of this changing attitude that their responsibilities in the future are largely concerned with individuals with long term illnesses with slow progression which require attitudes entirely different from what we were trained to have

Dr Meyer I would like to say a word in self defense or it may be that Dr Ross wasn't here when I spoke I set out what I thought we had observed about the inhibition on the spontaneity and interest of the consulting psychiatrist a senior clinician *in dealing with* elderly people and I particularly specified that not only for chronic illness but even in the process of acute breakdown in the elderly person we must include the physician himself as an object of study as he relate to the patient who is undergoing this experience

I would say that is has many practical ramifications and I *would* say too *speaking of* the practical ramifications that this withdrawal of interest—which is not easy to overcome no matter how hard you try—or feelings of discouragement may have very serious diagnostic implications that is many diagnoses of brain tumor or things that need medi

cal and surgical care are missed under the assumption that this is an old and arteriosclerotic person who is therefore naturally disturbed That is one very practical implication immediately, of the effect of the elderly sick person on the young physician

I would think too in relation to rigidity of elderly people, that we have to study the rigidity of the physician and the rigidity of the environment in which he works, because it seems to me that it is only honest to admit that on an acute busy medical service, with a house staff and young interns, regardless of the influence of the senior clinician and his interest an awful lot is going on on that ward that the visiting man doesn't know about and can t be there to influence

I rather think that there is a certain amount of irreconcilable and irreducible conflict between the interests and the needs of the busy medical service, dealing with acutely ill patients and the organization that might work best for the sick elderly person, who is not also disturbed I wonder—and Dr Seegal might wish to comment—if, without creating special geriatric units we might not have to think in terms of convalescent units, in which the sick elderly person s needs and the needs of the smooth working of a medical ward can more nearly mesh than on the service where both types of patients are in residence

CHAIRMAN CAMERON Any comment, Dr Seegal?

DR. SEEGAL. I think that the education of the medical student is enhanced by an opportunity to spend a sufficiently long period of time in an institution where patients are domiciled for a long period of time I would not say that they necessarily have to be geriatric patients It is hard enough to get personnel for a hospital for chronic illness I think you would find it extremely difficult to get the type of persons you wanted for all the hospitals limited just to geriatrics

But I entirely agree with you that a medical student has not been properly trained if his time is spent in looking at episodes of acute illness or acute episodes of chronic illness He doesn t get a chance to have his resources called upon He doesn t have a chance to suffer His patients are either well or dead within a week But that is not the practice of medicine The practice of medicine is having somebody transfer his problems, or have the family transfer their problems, to you over days months, or years That is the great burden on the pyhsician

CHAIRMAN CAMERON I think that Dr Zeman would like to comment.

DR ZEMAN I would like to get into this dicussion from the standpoint of our responsibility those of us who are here today on the platform and in the [illegible]
pract[illegible]
that [illegible]
don[illegible]
I [illegible]
and on the state society level [illegible]
kinds of reassurances about t[illegible]
little bit ashamed when they [illegible] are not able to cure them Many of these men feel frustrated and upset and don t like to see these patients for that reason Many of these men think that they are not really fulfilling their role as a physician if they just sit at the bedside and listen to the patient

among the old will take his best efforts A genuine liking for old people is a great asset Knowing the limitations of the aged organism the physician must be satisfied with limited goals He must realize and be quite content in the knowledge that palliation is in itself a worthy objective He must be aware of the dangers of overdosage with drugs He must be aware of the tremendous contributions that modern surgery can bring to his old people He must be particularly wary about overstaying time limits as far as elective operations are concerned

But I think that above all, the practicing physician needs to be taught that everything he does is psychotherapy The old intuitive methods were extremely useful What we used to belittle as a bedside manner, we now know had its therapeutic value But we are now more educated in these matters and physicians can learn simple rules of behavior simple rules of handling older people, which will be of great value to the patient and also of great value to the physician in making him feel that he is playing his own role to the full

CHAIRMAN CAMERON Thank you Are there any other questions which the Commission would like to put?

DR BOWMAN Dr Cameron my question is to Dr Métraux I point out that during these two days we have been discussing the old person and in general agreeing that our present way of dealing with the old person is not satisfactory It is harmful to him and to society And also it seems to be advanced that one of the important factors here is our cultural attitudes Dr Métraux, I believe so stated among other things and also stated that she felt that this cultural attitude could be changed I should therefore like to ask two questions

Firsts does she agree that the changing of our cultural pattern is one of the first and the most important steps for us to take in trying to deal really effectively with this whole situation?

Second how can we in a really practical way go about changing this cultural attitude? What suggestions would she make?

DR MÉTRAUX That is a large order Yes of course when we are talking about culture in a sense we are talking about abstractions The things we have been talking about here are content If we are talking about change of basic ideas etc we have to consider the problem of content of practical means of what the things we do convey in terms of this abstraction that we call culture

The suggestion here has been made—and again I come back to the point that was made and that I made before—that we include with our view the importance of progress in the on goingness of life if we try to find a number of varied places in which the older person fits in which the particular assets of the older person are fully recognized

When we talk about culture change we tend to think it might be as if we could just shift ideas Actually, what we are having to shift is actual practices and the fact that there are such symposia from which people can go home in the case of the physicians [illegible] more ar[illegible] [illegible]nk is the [illegible] different [illegible] ways

That, I should think on the whole, would answer the second part of your question also that we need to become articulate about what the problems are define them decide what kind of research we can do because certainly one of the extraordinary changes that has come about in the whole of the world in the last hundred years or so is that we

are able to articulate problems do research on them in fact to include thinking about what problems are and translate them back into daily life That is something which man has hardly done before on a large scale

CHAIRMAN CAMERON Thank you Does that answer it?

DR. BOWMAN Well I don t know I assume I asked what is relatively an impossible question to answer at a meeting like this and I suspect that I got about as much information as can be given I have a little of what you might call the discontent of one who wants to find a simple ready answer who feels rather certain there isn t any but who is hopefully trying

DR METRAUX Well I would include in that of course that we need to have a much more specific comparative understanding of the way in which people of different ages have been able to solve problems in different kinds of societies I included that in this formulation of what our particular problms are doing research and then taking that back into our daily solution of problems whatever our particular work is

CHAIRMAN CAMERON Well I certainly think it was a very good try on both sides Are there any other questions from the Commission?

DR WEINBERG Mr Chairman I would like to point up something that we are strug gling here with some difficulties in terms of definition of a culture by indicating the various streams of ideas that run in our society We seem to be bipolar in nature and antagonistic to each other so to speak but yet some aspects of the same stick

For in stance on the question of retirement nobody here has indicated in any sense that retirement may be a desirable state of affairs to many people Of course it has been said to some extent but we failed to recognize that retirement is a highly mot[illegible]

[illegible] to achieve In our society if you can retire at 65 it is a desirable state if you can do it at 45 you are a genius In a certain sense it has enor mous pull on us

Many a person works for early retirement without know[illegible]

In my experience cultural anthropologists, who have been so very wonderful in de lineating the various cultural patterns have nevertheless had extreme difficulty in de fining what began a certain type of cultural pattern They cannot describe the genesis of a culture They can describe how it operates For that reason I imagine it would be very difficult to state specifically what we can do to alter certain cultural attitudes in order to make our life more tolerable

CHAIRMAN CAMERON I have a question from the floor for Dr Zeman I know there are many very religious men on the panel but I am surprised that so little reference has been made to the role of religion in setting the stage for the approach of old age Would any member comment on the relative importance of religious activities or religion [illegible]ual s adjustment?

DR ZEMAN I have been very well aware for many years of the important role that religion plays in the lives of some people but more especially of the tremendous role that it has yet to learn to play in the lives of older people

I have had many talks with rabbis and ministers on this subject and many of them have expressed a good deal of interest in it but very few of them have really developed any constructive program

Actually there are two large ways in which the church may operate One is in a sense in physical way that is by using community houses and church premises for recreation centers and other sorts of activity for the older members of the neighborhood or of the particular church group Many are doing this But there is naturally a much broader role that they have to play in bringing to bear on the basic problem of life and death the message that religion aims to bring

The most outstanding contribution to this whole problem is the book *Old People and the Church* To me the most encouraging feature of the whole question is the fact that in theological schools of all denominations and all religions there is increasing emphasis being laid on pastoral counseling and on pastoral psychiatry

I think therefore as Dr Seegal has indicated that the medical students of the future are going to know more about old age so the religious leaders of the community are going to understand more intimately and more fundamentally the problems of old age that there can be no question at all that religion has a tremendous role to play and that that role at the present time as far as I know is only imperfectly realized

CHAIRMAN CAMERON I have time for only one more question as the hour is quite advanced This is directed to Dr Weinberg Have studies been made on clinically psychoneurotic persons in their twenties as to their adjustment after the age of 60?

DR WEINBERG I don t know of any such study We have attempted at Michael Reese Hospital to go back to our clinical records to pick up some of the people who were seen a number of years ago to determine what they had done with their lives and whether their early neurotic patterns had influenced the weight of their aging Unfortunately the records are of such a nature that it is almost impossible to get a clear cut picture as to the type of neurotic manifestations at that time due to the fact that many different people have examined the patients in the clinic and their conceptual formulation of what they had found certainly varies from many of our concepts of the present time so that it has been difficult

We are attempting to make a study a longitudinal study at present of some of the people beginning if you will at the age of 30 and up and keeping records of them at Michael Reese If we live long enough we might be able to see what we can do with them

[illegible] o incidentally
[illegible] k the members
[illegible] ens or to avoid
answering them as seemed most convenient I think they did exceedingly well and I would like to thank them on your behalf

PRESIDENT MOORE We haven t thanked the most important group of all namely the audience who have stayed with us during these two days and proved a most stimulating group of listeners

CONSTITUTION

AND

BY-LAWS

ASSOCIATION FOR RESEARCH IN
NERVOUS AND MENTAL DISEASE, INC.

1954

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE INC

CONSTITUTION

ARTICLE I

NAME

The Association shall be known as the Association for Research in Nervous and Mental Disease Incorporated

ARTICLE II

OBJECTS

The objects of the Association are to encourage, promote, foster and assist investigations and research in nervous and mental disease and to prepare print issue and distribute publications based upon such investigations and research

ARTICLE III

MEMBERS

The membership of the Association for Research in Nervous and Mental Disease Inc shall consist of Senior, Sustaining Active and Associate members

ARTICLE IV

OFFICERS

The officers of the Association shall be a President First Vice President, Second Vice President Secretary Treasurer and Assistant Secretary Treasurer The officers shall be elected by the members of the Association at the annual meeting to serve for one year

ARTICLE V

BOARD OF TRUSTEES

There shall be a Board of Trustees consisting of seven elected members with the President and Secretary Treasurer of the Association acting as ex officio members of the Board of Trustees The Board of Trustees shall elect one of its elected members as its Chairman

ARTICLE VI

COMMISSION

The members of the Commission shall consist of individuals appointed by the President and approved by the Board of Trustees, to serve for the

current year. The members of the Commission need not belong to the Association.

The Commission shall sit with the President at the annual meeting to hear the papers presented before the Association, may participate in the discussion of the contributions and question the authors of the papers presented before the Association.

ARTICLE VII

MEETINGS

The time and place of the annual meeting shall be determined by the Board of Trustees.

ARTICLE VIII

AMENDMENTS

Amendments to this Constitution shall be made in the following manner. The proposed amendment shall be presented in writing signed by at least three members of the Association and submitted to the Board of Trustees at least thirty days before the current annual meeting. At the current annual meeting the Board of Trustees shall report to the Association upon said proposed amendment with their recommendation. The amendment shall then be voted upon and two thirds of all votes cast at the meeting shall be necessary for the adoption of the amendment.

BY LAWS

ARTICLE I

ELECTION OF TRUSTEES DUTIES OF TRUSTEES

At each annual meeting a member of the Association shall be elected to the Board of Trustees by the Association for a term of seven years in the place of the senior member whose term then expires. Members of the Board of Trustees shall be eligible for re-election.

The Board of Trustees shall have general charge of the affairs, funds and property of the Association. It shall have full power and it shall be its duty to carry out the purposes of the Association according to the Charter, Constitution and By Laws. A majority of its members shall constitute a quorum.

The Chairman of the Board of Trustees shall be the Chief Executive Officer of the Association.

ARTICLE II

ELECTION OF OFFICERS DUTIES OF OFFICERS

The officers of the Association shall be elected by a majority of the members present at the Executive Session of the annual meeting and shall

serve for one year Officers shall be eligible for re-election Vacancies occurring in any office shall be filled by the Board of Trustees for the unexpired term until the next annual election

The President The President shall be responsible for the preparation of the scientific program shall preside at the annual meeting recommend to the Board of Trustees the appointment of the members of the Commission, call meetings of the Commission, and shall perform all duties customary to his office

The First Vice President In the absence of the President, the First Vice President shall discharge all the duties of the President

The Second Vice President In the absence of the President and the First Vice President the Second Vice President shall discharge all the duties of the President

The Secretary Treasurer The Secretary Treasurer shall issue notices of and keep records of the proceedings of all Executive and Scientific meetings of the Association and of the meetings of the Board of Trustees, shall notify officers members of the Commission and members of Committees of their election certify official records keep a list of members, issue notices of all meetings and perform all duties which may be required of him by the Board of Trustees the President and Vice Presidents He shall be responsible for and keep account of all funds of the Association and make disbursements as directed by the Board of Trustees

The Assistant Secretary Treasurer The Assistant Secretary Treasurer shall act as an assistant to the Secretary Treasurer and shall have power to act as the Secretary Treasurer in the absence or during any disability of the Secretary Treasurer

ARTICLE III

Nomination and Election of Members

Qualification for Election

All members in good standing of neurologic or psychiatric societies in the United States and Canada are eligible for membership in the various classes of membership of the Association upon being proposed by one and seconded by another member in good standing in the Association Proposals for election to membership must be reviewed by the Committee on Admissions and declared approved or disapproved Such favorable or unfavorable action shall be reviewed by the Board of Trustees and the Board of Trustees shall then elect by majority vote those individuals whom they approve Candidates acted upon unfavorably by the Committee on Admissions may be elected to membership by the unanimous vote of the Board of Trustees Candidates shall become members following election by the Board of Trustees and upon payment of dues

Sustaining and Active members shall be individuals who are engaged in the practice of clinical neurology, neurologic surgery or psychiatry Classification as a Sustaining or Active member depends upon the choice of the individual Associate members shall be individuals actively engaged full time in research work related to neurologic or psychiatric problems in recognized medical schools hospitals or research institutions

Individuals not fully qualified under the provisions of the preceding paragraphs may under special circumstances be elected to membership in the organization

Senior membership shall consist of those who have been members in good standing for twenty five years and who have reached the age of sixty five years Transfer to Senior membership of qualified Sustaining or Active members of the Association shall be optional Members in good standing not possessing the preceding qualifications may under exceptional circumstances be eligible for transfer to Senior membership at the discretion of the Board of Trustees

ARTICLE IV

Committees

A Nominating Committee of three members shall be appointed by the Chairman of the Board of Trustees prior to the annual meeting of the Association and the names of these members of the committee shall appear on the printed program It shall be the duty of the Nominating Committee to nominate a President First Vice President Second Vice President Secretary Treasurer Assistant Secretary Treasurer a member of the Board of Trustees a member of the Admissions Committee a member of the Committee on Public Relations and such other offices as the Association may from time to time desire

A committee on Admissions shall consist of three members each member to serve for a period of three years Each year a new member shall be elected at the Executive Session to replace the senior member of the Committee All proposals for membership shall be submitted to the Committee for recommendation and those that are approved by the Committee shall then be forwarded to the Board of Trustees for final action

An Auditing Committee of three members shall be appointed by the Chairman of the Board of Trustees prior to each annual meeting It shall be the duty of the Auditing Committee to examine the accounts of the Treasurer and to report to the Association at its annual meeting

A Committee on Public Relations shall consist of five members each member to serve for a period of five years Each year a new member of the Committee shall be elected at the Executive Session to replace the senior member of the Committee The Committee on Public Relations shall be

responsible for all matters of public relations particularly in connection with the lay and medical press and the relations of the Association with governmental and lay organizations

ARTICLE V

Meetings

The Executive Session of each annual meeting shall be arranged by the Board of Trustees and the scientific program shall be organized by the President of the Association Twenty five members shall constitute a quorum at the Executive Session at the annual meeting Robert s Rules of Order Revised, shall govern all meetings of the Association, except where otherwise specifically provided by the Constitution and/or By Laws of the Association

Meetings of the Board of Trustees shall be held whenever called by its Chairman or at the request of three of its members A majority of the Board of Trustees shall constitute a quorum

ARTICLE VI

Dues

The dues for Sustaining and Active members shall be determined annually by the Board of Trustees Senior and Associate members will not be subject to the payment of annual dues or assessments Dues may be remitted under special circumstances, by action of the Board of Trustees on request of an Active member

Any member who shall fail for one year to pay his dues, may, after due notification by registered letter from the Treasurer, have his name stricken from the list of members at the discretion of the Board of Trustees, unless said dues be paid within thirty days of the date of mailing the notice The Trustees shall be empowered to excuse any member from the payment of dues for reasons deemed by them to be good and sufficient

ARTICLE VII

Amendments

These By Laws may be amended in the same manner and with the same procedure as outlined for an amendment to the Constitution Amendments of the By Laws may also if urgently needed, be made by unanimous action of the Board of Trustees Such amendments however, to continue effective must be approved at the Executive Session of the next annual meeting of the Association

Revised and approved
at the Executive Session
on December 11, 1954

LIST OF MEMBERS

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

Sustaining Members—1955

Ebaugh Franklin C 1801 High St Denver 6 Colo
Gayle R Finley Professional Bldg 5th and Franklin Sts Richmond 19 Va
Greenberg I Melbourne 131 Fulton Ave Hempstead N Y
Hand B Marvin 269 S 19th St Philadelphia 3 Pa
Hoffman Leslie B Duke Medical School Durham N C
Kahn Edgar A 1313 E Ann St Ann Arbor Mich
Levy David M 15 E 91st St New York 28 N Y
Nielson Aage 10 Peterboro St Detroit 1 Mich
Teahan John W 889 Asylum Ave Hartford Conn
Terhune William B Silver Hill Foundation New Canaan Conn
Timme Walter Cold Spring Putnam County N Y
Zabriskie Edwin G 115 E 61st St New York 21 N Y

Senior Members—1955

Bond Earl D 111 N 49th St Philadelphia 39 Pa
Burley Benjamin T 19 High St Worcester Mass
Cannaday Royal G 121 E 60th St New York 22 N Y
Chamberlain Olin B Old Towne Rd Route 8 Charleston S C
Chaney J Beverley 3115 87th St Jackson Heights N Y
Cobb Stanley Massachusetts General Hospital Boston 14 Mass
Crothers Bronson 300 Longwood Ave Boston Mass
Davis Thomas K 70 E 77th St New York 21 N Y
Grant Francis C 3400 Spruce St Philadelphia 4 Pa
Huddleson James H 0620 S W Palatine Hill Rd Portland 1 Ore
Hunt Edward L 330 Ocean Ave Lawrence N Y
Keschner Moses 151 West End Ave New York 24 N Y
Mayer Edward E 5601 Forbes St Pittsburgh 17 Pa
[illegible]
Wallace Louis O S 119 Hall St Manchester N H
Weil Arthur 115-08 Park Lane S Kew Gardens N Y
Wholey Cornelius C 121 University Pl Pittsburgh Pa

Active Members—1955

Abbott John A Massachusetts General Hospital Boston 14 Mass
Abbott Kenneth H 3.0 E Broad St Columbus Ohio
Abbott Kenneth H 3.0 E Broad St Columbus Oh

ABRAMSON JOSEPH L 874 Park Place Brooklyn 16 N Y
ACKERLY SPAFFORD 206 E Chestnut St Louisville Ky
ADAMS RAYMOND D 3[illegible]0 Adams St Milton Mass
ADELSON EDWARD T 5[illegible] E 86th St New York 28 N Y
ADLER ALEXANDRA 30 Park Ave New York 16 N Y
ALAIMPRESE DONATO J 1226 13th Ave Altoona Pa
ALEXANDER EBEN JR Bowman Gray School of Medicine Winston Salem N C
ALEXANDER LEO 433 Marlborough St Boston Mass
ALPERS BERNARD J 111 N 49th St Philadelphia 39 Pa
AMES THADDEUS H 6301 N 52nd Pl Phoenix Ariz
A[illegible]OLS WILLIAM 710 W 168th St New York 3[illegible] N Y
ANDERSON JAMES L 2917 Coral Way Miami Fla
ANDERSON MILTON H State Hospital Evansville Ind
APPEL KENNETH E 111 N 49th St Philadelphia 39 Pa
ARANA ROMAN Convencion 128[illegible] Montevideo Uruguay
ARANOW HENRY JR 180 Ft Washington Ave New York 32 N Y
ARING CHARLES D Cincinnati General Hospital Cincinnati 29 Ohio
ARMSTRONG CATHERINE 87 S Highland Ave Ossining N Y
ARNOLD JESSE O 36 Pleasant St Worcester Mass
ARNOT ROBERT F 482 Beacon St Boston Mass
ARONSON STANLEY M 4[illegible]1 Clarkson Ave Brooklyn 3 N Y
ARZT PHILIP K 844 Lowry Medical Arts Bldg St Paul 2 Minn
ASCHER ABRAHAM H 27[illegible]5 Bedford Ave Brooklyn N Y
[illegible]ENJO ALFONSO G Casilla 1[illegible]31 Santiago Chile
AUSTIN JAMES University of Oregon School of Medicine Portland Ore
AYER JAMES B 319 Longwood Ave Boston Mass

BADAL DANIEL W University Hospital Cleveland 6 Ohio
BAILEY ORVILLE T 1315 W 10th St Indianapolis 7 Ind
BAILEY PEARCE National Institute of Neurological Diseases and Blindness National Institutes of Health Bethesda 14 Md
BAKER A B University of Minnesota Medical School Minneapolis 14 Minn
BALLANTINE H THOMAS JR Massachusetts General Hospital Boston 14 Mass
BALSER BENJAMIN H 8[illegible]2 Fifth Ave New York 21 N Y
BA[illegible]FORD THOMAS E JR 3 Stoneleigh Apt Bronxville N Y
BARD P[illegible] 710 N Washington St Baltimore 5 Md
BARNETT H J M 1[illegible]0 St George St Toronto Ontario Canada
BATKIN STANLEY University Hospital of the Good Shepherd Syracuse 10 N Y
BELL AARON 57 W [illegible]7th St New York 19 N Y
BENDER LAURETTA Bellevue Hospital 30th St & First Ave New York N Y
BENDER MORRIS B 11[illegible]0 Park Ave New York 28 N Y
BENNETT A E 2000 Dwight Way Berkeley 4 Calif
BERENS CONRAD [illegible]08 Park Ave New York 21 N Y
BERMAN [illegible]
BERMAN [illegible]
BERRY F [illegible]
BERTRAN[illegible]
B[illegible] [illegible] York [illegible] N Y
BLACK SAMUEL P W University of Missouri Hospitals Columbia Mo
BLAIN DANIEL 1[illegible]8[illegible] Massachusetts Ave N W Washington 6 D C
BL[illegible] ABRAM H 6[illegible]th Ave New York [illegible] N Y

Blustein Herman 6805 N Wolcott Ave Chicago 26 Ill
Bohn 7 Stephen 10 Peterboro Detroit Mich
Booth Carl B 500 W 235th St New York 63 N Y
Borkowski Winslow J 901 West Ave, Jenkintown Pa
Boshes Benjamin 760 N Michigan Ave Chicago 11, Ill
Botterell, E Harry, 280 Bloor St W Toronto 5 Canada
Bowman Karl M University of California Medical School San Francisco Calif
Braceland Francis J 200 Retreat Ave Hartford Conn
Bragdon Lloyd H Mercy Hospital Pittsburgh 19 Pa
Bremer Frederic 115 Blvd de Waterloo Brussels Belgium
Brickner Richard M 1000 Park Ave New York 28 N Y
Bridges Thomas J Jr 710 W 168th St New York 32 N Y
Brock Samuel 115 E 61st St New York 21 N Y
Brody, Bernard S 37 Trumbull St New Haven Conn
Brody Matthew 41 Eastern Pkwy Brooklyn N Y
Brosin Henry W 3811 O Hara St Pittsburgh 13 Pa
Brousseau Albert 103 Ave Henri Martin Paris France
Browder E Jefferson 200 Hicks St Brooklyn N Y
Brown Joe R 102 110 2nd Ave S W Rochester Minn
Brown Warren T 3220 Silver S E Albuquerque New Mex
Browne Mayers A N 55 E 86th St New York 28 N Y
Buckley Paul J 159 Palisade Ave Bogota N J
Buckley Richard C 111 Gillett St Hartford Conn
Bullard Dexter M Chestnut Lodge Rockville Md
Busse Ewald W Duke University School of Medicine Durham N C
Byers Randolph K 300 Longwood Ave Boston Mass

Cameron D Ewen Allen Memorial Institute of Psychiatry Royal Victoria Hospital
Montreal Canada
Campbell James B 630 W 168th St New York 32 N Y
Caner G Colket 63 Marlborough St Boston Mass
Carey Joshua H University of Michigan Ann Arbor Mich
Carey Thomas C 111 Gillett St Hartford 5 Conn
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